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RESEARCH ARTICLE

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Cortical dysfunction and impulsivity in non-suicidal self-injury: a multimodal study using TMS-EEG and fNIRS

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ABSTRACT

Objectives: This study aimed to investigate the cortical excitability differences between adolescents with NSSI and healthy controls using concurrent TMS-EEG and fNIRS.

Methods: Fifty-three participants aged 12–18 years were recruited, including 27 with NSSI and 26 healthy controls, matched for age. Independent samples t-tests were used to compare groups on the Adolescent Non-Suicidal Self-Injury Assessment Questionnaire (ANSAQ) and Suicidal Ideation Scale (SIOSS). fNIRS results were used to assess brain activation, and TMS-EEG was used to measure cortical excitability.

Results: The NSSI group exhibited significantly higher scores on both the ANSAQ and SIOSS compared to the healthy controls. fNIRS results showed reduced prefrontal and temporal lobe activation in the NSSI group. TMS-EEG analysis indicated heightened P30 amplitudes in the left and right prefrontal cortex in the NSSI group.

Conclusions: Adolescents with NSSI exhibit abnormal cortical excitability, particularly in the prefrontal regions, which may contribute to impulsive behaviors and cognitive control difficulties. This study highlights the potential of combining TMS-EEG and fNIRS to explore the neurophysiological substrates of NSSI, providing preliminary evidence that may guide future research on diagnostic and therapeutic strategies.

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Tms-EEG; fNIRS; NSSI; adolescents; cortical excitability

Introduction

Non-suicidal self-injury (NSSI) is an increasingly prevalent behavior among adolescents [1,2], characterized by deliberate self-harm without suicidal intent, such as cutting, burning, or hitting oneself [3]. Epidemiological data suggest that 15% to 20% of adolescents engage in NSSI at some point, highlighting it as a pressing public health concern [4].

Understanding NSSI requires a comprehensive approach that integrates psychological, social, and biological factors [5–7]. However, current assessments of NSSI predominantly rely on self-report questionnaires and clinical interviews, which are limited by subjectivity and reliability. Patients may minimize the severity of their self-injury due to shame or fear of judgment, and memory biases can further compromise the accuracy of self-reports. Additionally, traditional methods lack the depth needed to explore the neurophysiological mechanisms underlying NSSI, failing to identify objective biomarkers. These limitations hinder the precision of diagnoses and the effectiveness of interventions.

Recent advancements in non-invasive electrophysiological techniques, such as functional near-infrared spectroscopy (fNIRS) and transcranial magnetic stimulation concurrent with electroencephalography (TMS-EEG), provide promising opportunities to overcome these challenges [8,9]. fNIRS is a portable and cost-effective tool for measuring cerebral blood flow and brain activity, making it highly suitable for clinical applications. Research has demonstrated its potential in identifying brain activity patterns associated with various psychological states [8,10]. For example, Perlman et al. (2014) used fNIRS to investigate prefrontal activity related to frustration tolerance in young children, finding increased lateral prefrontal cortex activity during frustration that correlated with parent-reported frustration tolerance [11]. This underscores

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the role of the lateral prefrontal cortex in emotional regulation, a process often impaired in individuals with NSSI. Similarly, Husain et al. (2020) employed fNIRS to study adolescents with borderline personality disorder (BPD), revealing reduced activation in the frontal, temporal, and parietal cortices compared to healthy controls [12]. These finding suggest that fNIRS could be instrumental in detecting brain activity abnormalities associated with emotion dysregulation in NSSI. Similarly, TMS-EEG offers another valuable approach by enabling real-time monitoring of cortical excitability and connectivity [13–15]. For instance, Escamilla et al. (2018) used TMS-EEG to study the dorsomedial prefrontal cortex (dmPFC) during a fear-processing task, observing increased cortical excitability in response to threat stimuli. This heightened excitability was linked to structural integrity in the dmPFC and amygdala, indicating the utility of TMS-EEG in capturing dynamic changes related to emotional regulation [16]. Additionally, Alexandra et al. (2023) demonstrated the effectiveness of TMS-EEG in distinguishing Alzheimer's patients from healthy controls through distinct patterns in TMS-evoked potentials (TEPs) [17]. These studies underscore the potential of TMS-EEG to identify functional brain differences in psychiatric conditions, including NSSI.

This exploratory study aims to contribute to the understanding of NSSI by employing fNIRS and TMS-EEG to investigate its neurophysiological characteristics, providing preliminary evidence that may help address existing gaps in the field. By integrating these advanced techniques, we aim to explores potential neurophysiological correlates for NSSI and generates preliminary insights into diagnostic or therapeutic relevance.

Methods

Experimental procedure

In this study, we first estimated the effect size based on pre-experimental data. We conducted a priori sample size calculation (Cohen's d=1.01, alpha = 0.05, 1 – β=0.95), which indicated that 25 participants were required in each group to achieve sufficient statistical power. The experimental procedure involved a systematic approach to assess participants' mental health and neurophysiological characteristics. Upon their initial visit, each participant underwent a thorough clinical assessment conducted by a physician, which included a structured interview and the administration of relevant questionnaires. This was followed by electrophysiological evaluations to gather objective data on brain activity related to non-suicidal self-injury behaviors (Figure 1).

Participants

We initially recruited 32 adolescents for the NSSI group without severe psychiatric disorders but those who with mild comorbidities from the outpatient clinic of FanKang Clinic and the study was conducted from September 2024 to December 2024. However, two participants declined to participate in TMS-EEG

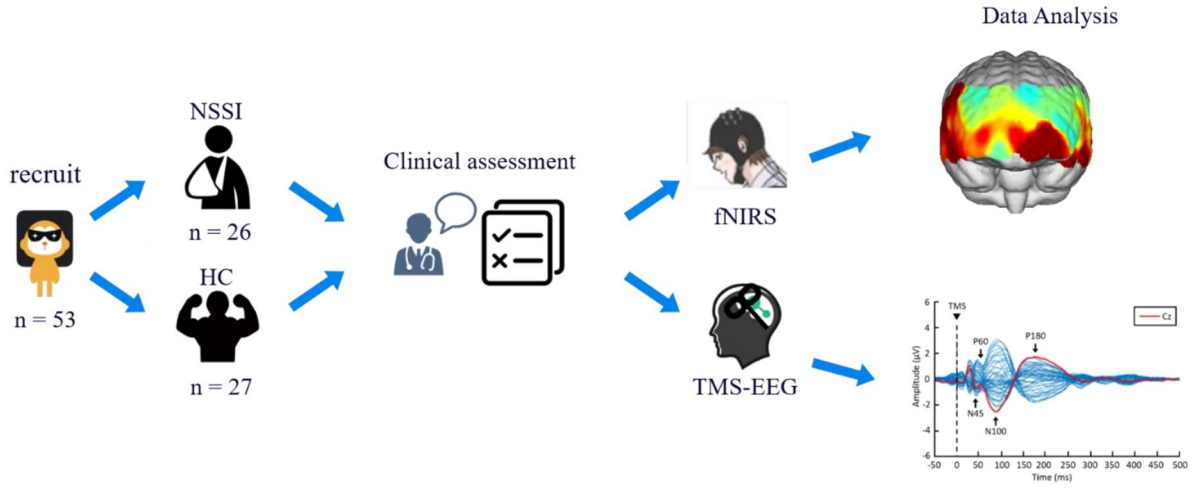

Figure 1. Experimental flowchart. The process begins with participants' initial visit, followed by clinical assessments, and then the collection of fNIRS and TMS-EEG data.

data collection, two did not meet the inclusion criteria, and one experienced discomfort during the assessment and withdrew from the study. As a result, 27 participants from the NSSI group completed the data collection and were included in the analysis.

The inclusion and exclusion criteria for this study were adapted from previous research and tailored to the specific aims of the study [18,19]. The inclusion criteria were as follows: (1) adolescents aged 12 to 18 years; (2) a score of 5 or higher on the Adolescent Non-Suicidal Self-Injury Assessment Questionnaire (ANSAQ) and self-reported engagement in at least one episode of self-injury behavior within the past month; (3) full understanding of the Chinese language, and the ability to participate in regular treatment. Exclusion criteria included: (1) the presence of severe psychiatric disorders or major physical illnesses, as assessed by a senior psychiatrist; the severe psychiatric disorders specifically refer to schizophrenia spectrum disorders (including schizophrenia, schizoaffective disorder, schizophreniform disorder, and delusional disorder), major depressive disorder or bipolar disorder with psychotic features, organic mental disorders directly caused by identifiable medical conditions (e.g. brain tumors, severe epilepsy, encephalitis, metabolic disturbances, severe endocrine disorders) or substances (drugs/medications) manifesting as psychotic symptoms, severe consciousness disturbances (e.g. delirium) or significant cognitive impairment (e.g. dementia), as well as neurodevelopmental disorders with severe behavioral dysregulation or psychotic symptoms (including intellectual disability with severe aggression/self-injury/psychotic features and autism spectrum disorder with comorbid psychotic symptoms), and acute severe mental states such as delirium or severe substance intoxication/withdrawal with psychotic symptoms. Disorders typically not classified as 'severe' in this context include major depressive disorder without psychotic features, bipolar disorder without current psychotic features, post-traumatic stress disorder, obsessive-compulsive disorder, eating disorders (e.g. anorexia nervosa, bulimia nervosa), conduct disorder, oppositional defiant disorder, and borderline personality disorder. (2) current use of medications that affect the central nervous system, with the exception of prescribed psychiatric medications (e.g. Sertraline, Quetiapine, Lamotrigine, Oxazepam); (3) inability to understand Chinese and engage in the treatment protocol. And the inclusion criteria for healthy controls were: (1) not meeting DSM-5 diagnostic criteria for psychiatric disorders such as schizophrenia, nor having relevant medical history; (2) no history of psychotropic medication use; (3) absence of suicidal behaviors with suicidal ideation scale scores below 12 and non-suicidal self-injury questionnaire scores below 5.

For the healthy control group, 29 adolescents were recruited from the public, but one declined participation in the TMS-EEG assessment, one withdrew during the assessment, and one was withdrawn by a guardian. Therefore, the final sample size for the healthy control group was 26. All participants provided written informed consent and guardian consent before participating in the study. The study was approved by the Medical Ethics Committee of Jinhua Second Hospital (2024-05-002) in the Second Hospital of Jinhua on September 4, 2024, and conducted in accordance with the Declaration of Helsinki.

Clinical assessment

Participants completed two key self-report measures: the Suicidal Ideation Scale (SIOSS) and the ANSAQ, which were evaluated by a same senior psychiatrist.

SIOSS: This scale comprises 26 items assessing suicidal ideation across four dimensions: optimism, sleep, hopelessness, and disguise. A total score of 12 or higher indicates the presence of suicidal thoughts.

ANSAQ: This 12-item questionnaire evaluates the frequency and severity of NSSI behaviors and has shown good reliability and validity.

Alongside these questionnaires, a self-developed demographic questionnaire was administered to collect information about participants' family and clinical histories.

Electrophysiological assessments

fNIRS assessment

A 48-channel near-infrared spectroscopy system (NirScan-6000C equipment, Danyang Huichuang Medical Equipment Co., Ltd., China) was employed to measure changes in oxyhemoglobin (HbO) and deoxyhemoglobin (HbR) concentrations [10]. Participants were seated comfortably in a quiet environment and

fitted with a detection cap prior to the task. The Verbal Fluency Task (VFT) [20–22], one of the most widely used cognitive tasks in fNIRS research, was conducted to assess participants' executive functions and verbal abilities. The VFT lasted for 3 min and consisted of alternating counting and word-generation phases. During the task, participants were prompted to repeat simple numerical sequences (e.g. '1-5') based on auditory cues, followed by a word-generation task where they created as many words as possible using a given prompt syllable (e.g. '火'). Each word-generation phase lasted 20 s, and three prompt syllables were used sequentially [22]. After completing the word generation, participants returned to counting until the task concluded.

EEG recording

TMS-evoked potentials (TEPs) were recorded using a 21-channel EEG system (BE PLUS PRO ADVANCED, EBneuro, Italy) with a sampling rate of 2048 Hz. The FCz electrode was used as the reference, and Fpz served as the ground electrode. Participants were seated comfortably in a relaxed state, with their gaze directed forward. Single-pulse TMS was applied to the F3 electrode site at 100% of each participant's resting motor threshold (RMT). The TMS coil was positioned tangentially to the scalp, with its central axis oriented at a 45° to the sagittal plane of the brain, and the handle directed posteriorly [23]. The RMT was defined as the minimum stimulation intensity that elicited a visible motor response in the first dorsal interosseous (FDI) muscle in at least 5 out of 10 trials while the muscle was at rest [9]. Stimulation was delivered at 8-second intervals, with a total of 80 pulses [24] administered using an 8-shaped TMS coil (70 mm, M-100 Ultimate, Shenzhen Yingchi Technology co., Ltd., China), it does not alter cortical motor excitability when a single-pulse TMS is delivered to the same location with an interstimulus interval exceeding 3 seconds [25,26].

Data analysis

fNIRS data

We use the NirSpark software package (Huichuang, China) for data processing. Initially, the raw light intensity signals recorded by the fNIRS system were converted into optical density (OD) values to account for light attenuation through tissues. These OD signals were then transformed into HbO and HbR concentrations using the modified Beer-Lambert law, incorporating path length correction factors. Motion artifacts caused by head or body movements during the task were identified and corrected using wavelet-based filtering techniques to minimize non-neural artifacts (Str_thr = 6, Amp_thr = 0.5). Subsequently, the data underwent low-pass filtering to remove high-frequency noise, such as cardiac pulsations, and high-pass filtering to eliminate slow baseline drifts, enhancing signal quality (High = 0.01 Hz, Low = 0.2 Hz). Channels with poor signal-to-noise ratios were assessed, and either excluded from further analysis or interpolated to maintain data integrity. The data were then segmented into task-related blocks, with these segments averaged across repetitions to improve the signal-to-noise ratio and highlight task-induced neural activity [27]. We selected a 60 s time window during the task state and computed the average change in HbO concentration.

TMS-EEG data analysis

The preprocessing of TEPs data was performed using custom scripts in MATLAB (R2017a, the MathWorks, USA), utilizing the TMS-EEG Signal Analyzer (TESA) toolbox. The analysis involved several sequential steps to ensure the removal of artifacts and the extraction of clean neural signals [28]. First, TMS-evoked waveforms were identified and marked. The data were segmented into time windows (−1000ms to 1000 ms) around the TMS pulse, followed by baseline correction (−500ms to 0 ms). The segmented data were then down sampled to 1000 Hz to reduce computational load. Next, an initial Independent Component Analysis (ICA) was conducted to remove artifacts associated with TMS-induced muscle activity and decay artifacts. Following the first ICA, the data were inspected for bad channels and problematic segments, which were subsequently addressed. After these initial corrections, the data were filtered (bandpass = 1–80 Hz; bandstop = 48–52 Hz) and subjected to a second ICA. This secondary ICA targeted non-neural artifacts, including those arising from eye blinks, eye movements, auditory artifacts, electrode noise, and

other non-neural signals [13,29]. Once the ICA steps were completed, the previously removed channels were reinserted, and then the data were re-referenced to the common average.

Statistical analysis

Statistical analyses were performed using SPSS (IBM Corp, Armonk, NY, version 26) software. Descriptive statistics were first calculated to summarize the demographic characteristics of the participants. To assess gender differences between the two groups, a Chi-square test was performed. For continuous variables, the Shapiro-Wilk test was applied to examine the normality of data distributions. Independent sample t-tests were conducted to compare the differences in questionnaire scores and electrophysiological measures between the two groups. For the TMS-EEG data analysis, specific channels were selected for region of interest (ROI) statistical analysis. The left frontal lobe was represented by the following channels: 'F3, C3, F7, FP1', while the right frontal lobe was represented by the channels: 'F4, C4, F8, FP2'. We extracted TEP data from four individual channels and subsequently performed signal averaging across these channels. Additionally, Pearson's correlation analyses were used to examine the relationships between questionnaire scores and electrophysiological indices. Because of HC participants showed meaningful variance in ANSAQ scores, our correlation analysis includes both NSSI and HC groups. All statistical tests were two-tailed and considered statistically significant if the p-value was less than or equal to 0.05.

Results

Demographic characteristics of the participants

Table 1 presents the demographic characteristics of the two groups. Independent sample t-tests and chi-square tests were conducted to compare the groups on age and gender. The results indicated no significant differences between the NSSI and healthy control groups in terms of age ($t = 1.122$, $p = 0.267$) and gender distribution ($\chi^2 = 0.498$, $p = 0.480$) (Table 1).

Self-report measures

Independent samples t-tests showed significant differences between the NSSI group and healthy controls in both SIOSS and ANSAQ scores. The NSSI group reported higher levels of suicidal ideation compared to the healthy group (M[SD], NSSI, 14.33[3.98]; HC, 4.77[3.04]; $t = 9.81$, $p < 0.0001$). Similarly, the NSSI participants scored higher on the ANSAQ than their counterparts (M[SD], NSSI, 12.56[5.52]; HC, 0.88[1.18]; $t = 10.73$, $p < 0.0001$) (Figure 2).

fNIRS results

Analysis of fNIRS data revealed significant differences in the integral values of the frontal and temporal lobes between the NSSI and HC groups. The integral values, which represent the total cerebral blood flow activity in these regions during the task, were significantly lower in the NSSI group compared to the HC group. Specifically, the NSSI group exhibited reduced frontal lobe activation ($M[SD]_{frontal}$, NSSI, 19.87[93.48]; HC, 109.4[93.95]; $t = -3.48$, $p = 0.001$) and temporal lobe activation ($M[SD]_{temporal}$, NSSI, 21.96[81.89]; HC, 80.18[74.54]; $t = -2.7$, $p = 0.009$) (Figure 3).

TEPs analysis

Quantification of TEP components at the F3 electrode using an average amplitude algorithm to probe the electrophysiological activity induced by TMS pulses at the stimulation site. TEPs analysis showed significant differences in the P30 component in the left and right frontal regions, with the NSSI group displaying significantly higher P30 amplitudes than the healthy group ($M[SD]_{left}$, NSSI, 1.95[1.57]; HC, 0.69[0.79]; $t = 3.72$, $p = 0.0006$; $M[SD]_{right}$, NSSI, 1.81[1.29]; HC, 1.00[0.76]; $t = 2.76$, $p = 0.0086$). There were no significant differences in other components: the N45 ($M[SD]_{left}$, NSSI, 1.09[1.18]; HC, 0.73[0.57]; $t = 1.41$, $p = 0.166$; $M[SD]_{right}$, NSSI, 0.86[0.83]; HC, 0.95[0.81]; $t = -0.42$, $p = 0.68$) or N100 ($M[SD]_{left}$, NSSI,

Table 1. Demographic and clinical characteristics of the participants.

Variable	NSSI ($n=27$)	Healthy controls ($n=26$)	t/χ^2	p value
Demographics				
Age (years, M ± SD)	15.04 ± 1.53	14.54 ± 1.70	1.122	0.267
Sex (male:female)	6:21	8:18	0.498	0.480
Condition				
Disease course (/weeks)	84.37 ± 46.91	–	9.346	<0.0001
NSSI duration (/weeks)	64.74 ± 43.71	4.15 ± 6.29	7.127	<0.0001
Co-occurring diagnoses (n = 27)	Number			
Impulse Control Disorder (ICD)	1	–		
Bipolar Disorder (BD)	7	–		
Depressive Disorder	10	–		
Anxiety Disorders	2	–		
Adjustment Disorder (AD)	4	–		
Attention-Deficit/Hyperactivity Disorder (ADHD)	1	–		
Obsessive-Compulsive Disorder (OCD)	1	–		
Post-Traumatic Stress Disorder (PTSD)	1	–		
Medications ($n=15$)	Discontinued (>1 Month)/Continued			
Sertraline/Quetiapine	2/5	–		
Atomoxetine /Aripiprazole	1/1	–		
Fluoxetine	1/1	–		
Lamotrigine/Oxazepam	0/1	–		
Lithium Carbonate	1/0	–		
Fluvoxamine	0/2	–		
Primary outcomes				
ANSAQ	12.56 ± 5.52	0.88 ± 1.18	10.733	<0.0001
SIOSS	14.33 ± 3.98	4.77 ± 3.04	9.806	<0.0001
Prevalence of NSSI and SI				
NSSI	92.6%	–		
SI	70.4%	–		

Note: NSSI = Nonsuicidal self-injury, ANSAQ = Adolescent Non-Suicidal Self-Injury Assessment Questionnaire, SIOSS = Suicidal Ideation Scale. p values indicated comparisons between two groups.

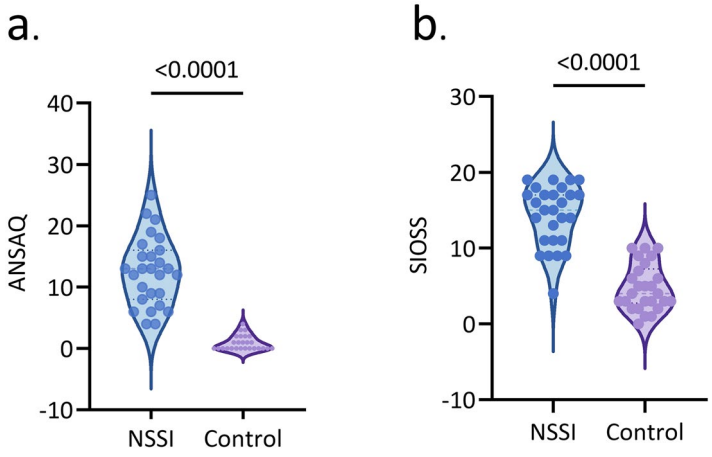

Figure 2. Clinical results. The NSSI group exhibited significantly higher self-injury behaviors ($t=9.81$, $p<0.0001$) and suicidal ideation ($t=10.73$, $p<0.0001$) compared to the healthy control group.

3.29[2.33]; HC, 2.50[2.58]; $t=1.17$, $p=0.247$; $M[SD]_{right}$, NSSI, 2.65[1.93]; HC, 2.12[1.56]; $t=1.11$, $p=0.271$) (Figure 4).

We performed additional correlation analyses within the NSSI group. However, no significant correlations were found in the NSSI-only analysis (all $p>0.05$).

Discussion

This study aimed to explore the neurophysiological mechanisms underlying NSSI in adolescents by utilizing advanced electrophysiological techniques, specifically TMS-EEG and fNIRS. Specifically, the NSSI group scored significantly higher on both the self-injury behavior scale and the suicidal ideation scale compared to the healthy control group. Regarding the fNIRS data, we found that the NSSI group

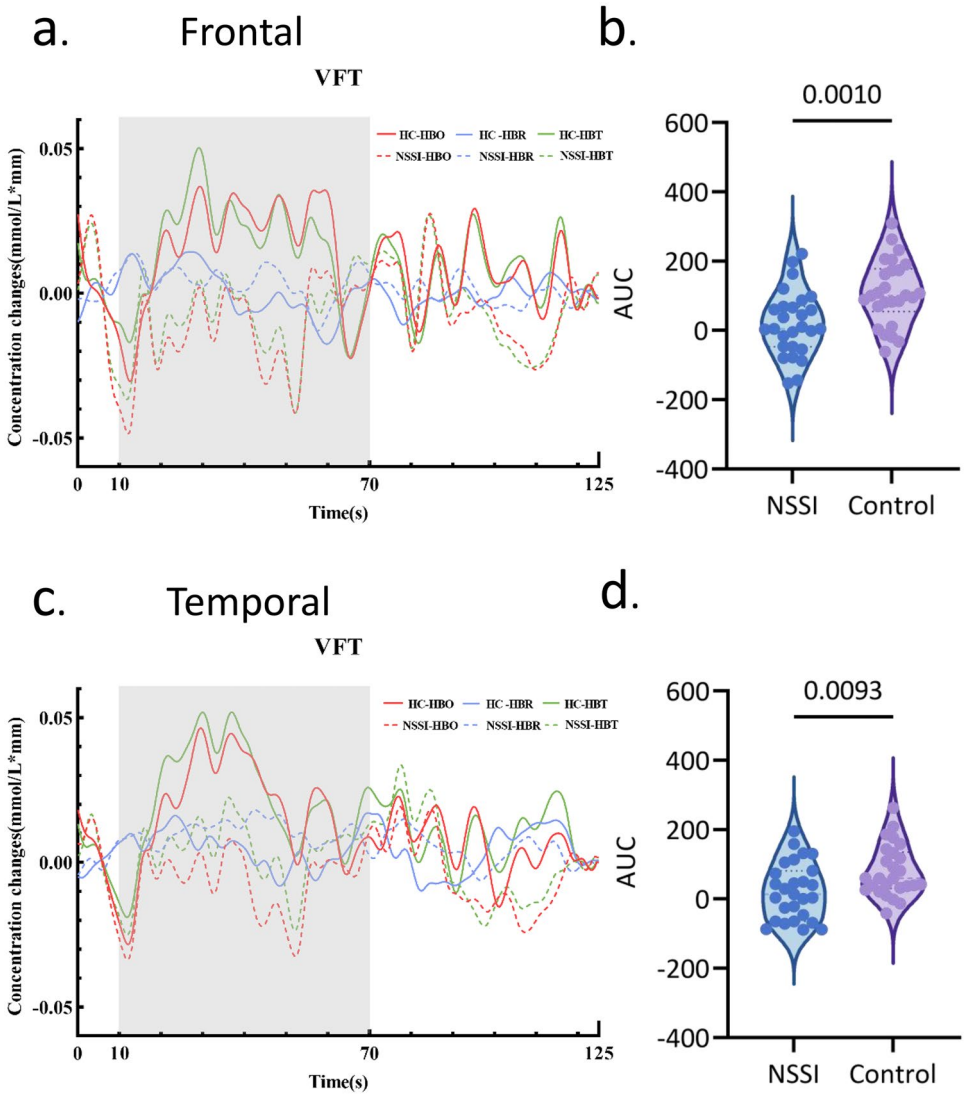

Figure 3. fNIRS Integral value results. (a) Prefrontal HbO/HbR change curves. (b) The NSSI group showed significantly lower integral values in the frontal compared to the healthy control group ($t = -3.48$, $p = 0.001$). (c) Temporal HbO/HbR change curves. (d) The NSSI group showed significantly lower integral values in the temporal lobes ($t = -2.7$, $p = 0.009$) compared to the healthy control group.

exhibited significantly lower integral values in both the frontal and temporal lobes compared to the control group. In the TEP analysis, we observed significantly higher P30 amplitudes in both the left and right frontal lobes of the NSSI group compared to the healthy controls.

In this cross-sectional study, we found that adolescents in the NSSI group exhibited significantly higher levels of suicidal ideation and self-injury behaviors compared to the control group. Adolescents engaging in NSSI reported higher levels of suicidal ideation and self-injury behaviors, reinforcing the link between self-harm and psychological distress. The observed differences in self-reported measures highlight the psychological complexity of NSSI. The elevated levels of suicidal ideation within the NSSI group suggest that many adolescents use self-injury as a maladaptive coping strategy to manage overwhelming emotions or psychological pain. Previous studies have supported this notion, particularly research by Nock (2009), which suggests that self-injury can be conceptualized as a mechanism to regulate intense emotional states [30]. Nock's model highlights how self-injurious behaviors are often used to reduce negative emotions such as sadness, anxiety, or frustration [30]. Similarly, Klonsky (2007) found that individuals who engage in NSSI often report using it as a way to feel relief or control over their emotions, supporting the idea that self-injury is employed as a maladaptive coping strategy [31]. These findings corroborate our results, providing further evidence for the role of NSSI in emotional regulation.

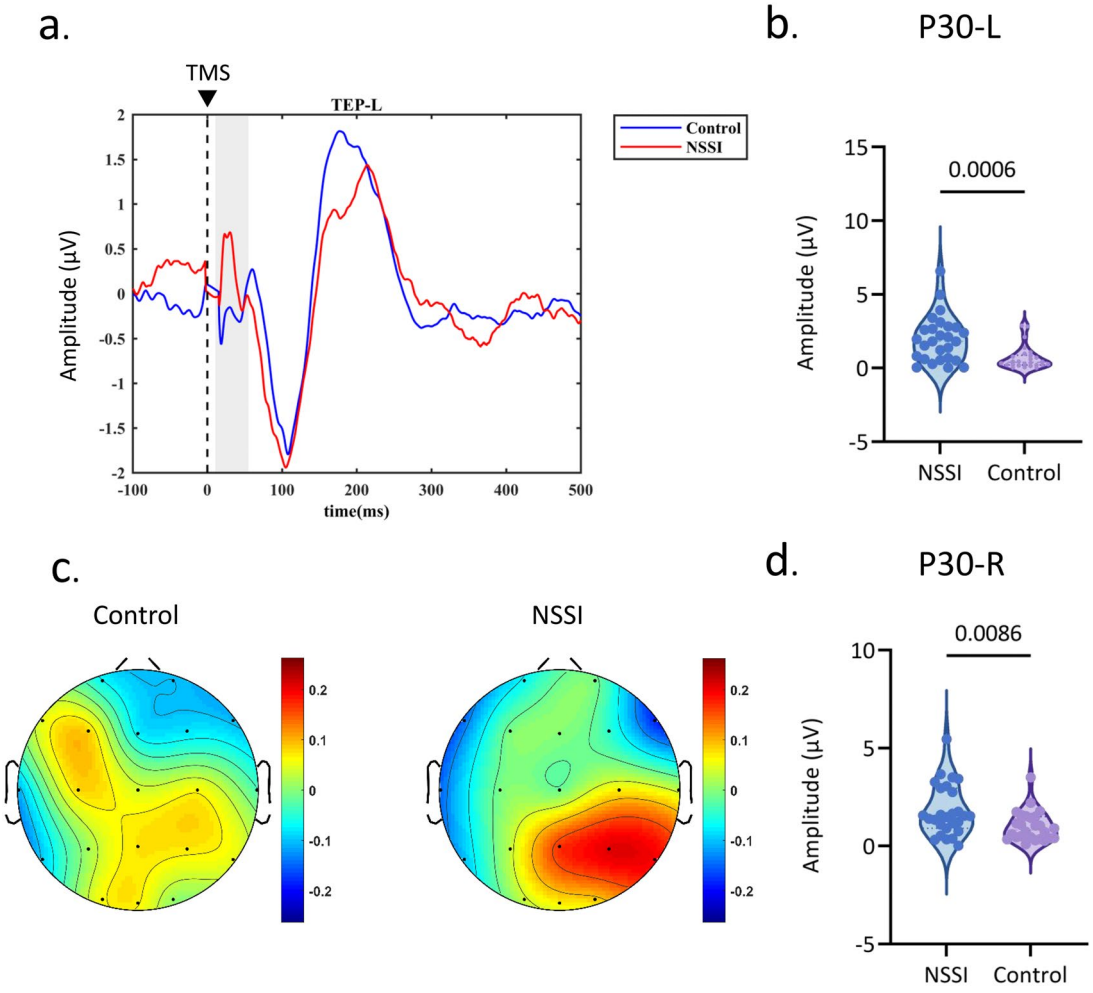

Figure 4. TMS-EEG Results. (a) The EEG waveform plots. (b) The NSSI group exhibited significantly higher P30 amplitudes in left frontal lobe ($t = 3.72$, $p = 0.0006$) compared to the healthy control group. (c) The EEG scalp topography maps. (d) The NSSI group exhibited significantly higher P30 amplitudes in right ($t = 2.74$, $p = 0.0086$) frontal lobe compared to the healthy control group.

The NSSI group exhibited significant differences in the integral values of the frontal and temporal lobes compared to the control group during the fNIRS VFT task, with the NSSI group showing lower activation, particularly in the prefrontal cortex, which plays a critical role in cognitive control, emotional regulation, and decision-making [20,32,33]. While negative HbO integral values may seem counterintuitive, it is crucial to recognize that fNIRS technology measures relative changes in hemoglobin concentrations (HbO and HbR) from baseline rather than absolute levels. A negative HbO integral indicates an overall slight decrease during the task relative to baseline, which may stem from inter individual variability in hemodynamic regulation that a phenomenon particularly common in adolescent populations. In our study design, the baseline was established during a 10 s pre-task rest period. Some participants might have exhibited spontaneous prefrontal activation during this 'rest' phase (e.g. through internal verbalization or anticipatory responses), potentially elevating the baseline and consequently creating an apparent 'relative decrease' during task performance. Furthermore, existing literature confirms that HbO decreases during verbal fluency tasks (VFT) are not uncommon [34,35]. In recent studies, Case et al. (2020) found that NSSI was associated with decreased activation in the prefrontal cortex during reward processing tasks, even after controlling for depressive symptoms, suggesting that NSSI may disrupt neural circuits involved in emotional and cognitive regulation [36]. Similarly, Young (2019) highlighted in a review of neuroimaging studies that adolescents with mood disorders often show altered amygdala-prefrontal cortical connectivity, a key neural circuit involved in emotion regulation [37]. These findings align with our results, indicating that dysfunction in the prefrontal cortex likely contributes to

impaired emotional regulation and maladaptive coping strategies, such as NSSI, in adolescents. Additionally, decreased temporal lobe activity was observed in the NSSI group. The temporal lobe, involved in memory, language processing, and social cognition, has not been extensively studied in NSSI, but it plays a critical role in processing emotional and social information [38–40]. Garcin et al. (2015) found that the right anterior temporal lobe is involved in cognitive tasks such as categorization, with its activation linked to the processing of social and emotional information [39]. Similarly, Schurz et al. (2014) reviewed social-cognitive processes, showing that the temporal lobe plays a key role in empathy and theory of mind, both of which are critical for understanding others' emotional states and regulating social behavior [38]. Furthermore, Spitsyna et al. (2006) demonstrated that verbal comprehension, which involves emotional and social processing, converges in the anterior temporal cortex, further emphasizing the role of the temporal lobe in integrating emotional and cognitive processes [40].

In the TMS-EEG analysis, significant differences were found in the P30 component of the TEP between the NSSI and control groups, with the NSSI group exhibiting a higher amplitude. Early TMS-evoked potentials, such as the P30 component, have been linked to excitatory activity in the cortex. Komssi et al. (2004) found that as TMS intensity increased, the amplitude of the P30 component rose in a sigmoidal fashion, reflecting heightened cortical excitability during early sensory processing [41]. Similarly, the results from Casula et al. (2024) suggest that the P30 may reflect initial sensory processing and cognitive control functions [42]. The elevated amplitude in the NSSI group suggests heightened sensitivity or altered processing of external stimuli, manifesting as more impulsive behavior, which could be indicative of emotional dysregulation commonly observed in individuals engaging in NSSI behaviors. This finding aligns with previous studies indicating that individuals with emotional dysregulation tend to exhibit exaggerated neural responses to stimuli, potentially contributing to maladaptive coping behaviors [31]. On the other hand, in a study by Van Der Werf and Paus (2006), repetitive transcranial magnetic stimulation (rTMS) applied over the primary motor cortex was shown to influence the N45 amplitude, with modulation leading to changes in cortical excitability, but without significantly enhancing inhibitory responses [43]. Similarly, Casula et al. (2014) found that low-frequency rTMS over the primary motor cortex increased the N100 amplitude, which is believed to reflect GABA-mediated inhibitory post-synaptic potentials [44]. However, they observed no changes in N45 or enhanced inhibitory control in their sample following rTMS. From the perspective of the balance between cortical excitation and inhibition, the observed heightened early cortical excitability in the NSSI group may indicate a need for stronger inhibitory control to counterbalance the increased excitatory activity, which could otherwise contribute to impulsive self-injurious behavior. Our data found no significant differences in the N45 or N100 components between the two groups, suggesting that the NSSI group does not show any enhanced inhibitory control. This absence of compensatory inhibitory strength may help explain the tendency toward recurrent self-injury in adolescents with NSSI.

While the combination of 'reduced prefrontal activation (fNIRS)' and 'enhanced cortical excitability (TMS-EEG)' may initially seem paradoxical, these measures reveal complementary dimensions of brain function in NSSI individuals, collectively advancing our understanding of their neurophysiological mechanisms. First, fNIRS and TMS-EEG assess fundamentally distinct neural processes. fNIRS captures sustained metabolic and hemodynamic demands during cognitive tasks, serving as an index of task engagement, whereas TMS-EEG measures transient electrophysiological responses to external stimulation (e.g. TMS pulses), reflecting the excitation/inhibition balance in resting or low demand states. Second, this coexistence of 'reduced task activation and enhanced stimulus reactivity' may represent a 'hyporegulated but hypersensitive' functional state. Specifically, the prefrontal cortex shows diminished mobilization during cognitive/emotional tasks (reduced HbO response) yet exhibits exaggerated reactivity to external stimuli (enhanced P30 amplitude). This pattern aligns with previous neuroimaging findings in borderline personality disorder and impulse control disorders, characterized by weakened top-down control coupled with bottom-up hyperreactivity. Third, this configuration may reflect a 'cortical dysregulation' state in NSSI adolescents that deficient baseline regulatory activation but excessive sensitivity to external stimuli. Such neural profile could underlie their emotional hyperreactivity, impaired cognitive control, and propensity for self-injurious coping strategies.

We found no significant correlations specifically within the NSSI group, which may be attributable to insufficient sample size or restricted distribution ranges. Future studies with larger samples or continuous symptom distribution approaches are needed to further explore these findings.

Our data revealed that individuals with NSSI exhibited significantly reduced prefrontal/temporal activation on fNIRS alongside elevated P30 amplitudes on TMS-EEG. These findings suggest that NSSI adolescents may present a distinct neurophysiological profile characterized by impaired emotion regulation and heightened stimulus reactivity. Consequently, these electrophysiological measures hold clinical promise for identifying candidates suitable for emotion-regulation-focused interventions (e.g. emotion recognition training, DBT), monitoring neural response changes during treatment, evaluating intervention efficacy, and developing prefrontal targeted non-pharmacological therapies (e.g. personalized TMS protocols). Furthermore, while conventional NSSI assessments predominantly rely on subjective self-reports and clinical interviews that are susceptible to response biases, concealment tendencies, and memory distortions, our study reveals that electrophysiological measures can detect prefrontal activation and P30 response variations even among individuals with comparable symptom scores, thereby suggests that electrophysiological measures may represent candidate markers of altered prefrontal function. At present, such measures should be considered exploratory and require validation in larger, longitudinal studies before any clinical application. We therefore recommend incorporating fNIRS or TMS-EEG as complementary neurophysiological assessment tools to augment traditional evaluation methods, facilitating early screening in high-risk populations, objective assessment of cognitive emotional functioning, and potential development of integrated biopsychosocial subtyping models.

Limitations

While this study provides valuable insights into the neural mechanisms underlying NSSI, there are a few limitations that must be considered. First, adolescents with NSSI typically exhibit high comorbidity rates with other psychiatric disorders, our study specifically excluded NSSI participants with severe psychiatric disorders may limit the generalizability of the findings. Future studies with larger and more diverse samples are needed to confirm these results. Second, the cross-sectional design of the study restricts our ability to draw causal conclusions regarding the relationship between brain activity and self-injury behaviors. Longitudinal research would be helpful in understanding how changes in brain function over time may contribute to the onset and persistence of NSSI. For the VFT task, we focused exclusively on electrophysiological measures and did not collect behavioral data. Future studies should incorporate behavioral performance metrics alongside electrophysiological measures. The last, throughout the study, we did not discontinue medications for patients who were already on drug regimens. However, certain psychiatric medications may influence the nervous system. Although the number of patients on continuous medication was small, this suggests that results should still be interpreted with caution. Future research should fully account for the additional effects of medication in both experimental design and data interpretation.

Conclusion

This study is the first to combine fNIRS and TMS-EEG techniques to reveal functional deficits in the frontal and temporal lobes, as well as abnormalities in the P30 component in adolescents with NSSI. This study provides preliminary evidence of altered prefrontal/temporal activity and P30 responses in adolescents with NSSI. These results generate hypotheses about potential neurophysiological markers and establish groundwork for future research. Large-scale, longitudinal studies will be necessary to determine whether such measures can eventually contribute to improved diagnostic precision or inform individualized interventions.

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BT, TY contributed to conceptualization, data curation, formal analysis, investigation, writing - original draft preparation and writing - review & editing. PX, LS, YN, LH contributed to investigation. CT contributed to conceptualization, supervision, and writing - review & editing. All authors have read and approved the final version of the manuscript.

Author contribution statement

CRediT: **Bolin Tan**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing; **Chunnan Tong**: Conceptualization, Data curation, Project administration, Resources, Supervision, Writing – review & editing; **Peng Xie**: Investigation, Project administration, Resources, Software, Validation; **Linfei Shou**: Investigation, Project administration; **Yue Ning**: Investigation, Project administration, Resources; **Lirong Hu**: Investigation, Project administration, Resources; **Tianyi Yuan**: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing.

Disclosure statement

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Data availability statement

All the data and codes generating findings of this work are available upon the request from the corresponding author.

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