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Impulsivity in Major Depressive Disorder Patients with Suicidal Ideation: Event-related Potentials in a GoNogo Task

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Objective: Suicidal ideation is one of the strongest predictors of suicide, and its relevance to impulsivity in depressed patients has been accumulated. Furthermore, high impulsivity patients show the attenuation of the Nogo amplitude in the GoNogo event-related potential (ERP). The purpose of the current study is to determine the correlation of Nogo ERP to the suicidal ideation depending on the condition of its presence or absence in major depressive disorder (MDD) patients.
Methods: A total 162 participants (104 patients with suicidal ideation, 31 patients without suicidal ideation, and 27 healthy controls) were recruited, and performed GoNogo tasks during the electroencephalogram measurement. Depression, anxiety, suicidal ideation and impulsivity were assessed by self-rating scales. The clinical measures, behavioral data and Nogo ERP were compared among groups.
Results: The MDD with suicidal ideation (SI) group showed significantly decreased Nogo P3 amplitudes compared to MDD without SI (Fz and Cz electrodes) and control group (all electrodes). The MDD with SI group also had significantly low accuracy of both Go and Nogo trails, compared to the MDD without group. The Nogo P3 amplitudes showed the negative relation to the scores of impulsivity, depression, anxiety and SI.
Conclusion: Our results concluded that the Nogo P3 ERP amplitude was decreased in MDD patients with SI compared to MDD patients without SI and controls. These findings suggest that the decreased Nogo P3 amplitude is the one of the candidate biomarker for impulsivity in MDD patients to evaluating SI.

KEY WORDS: Impulsivity; Suicidal ideation; Suicide; Major depressive disorder; Event-related potentials.

INTRODUCTION

The increase of the suicide rates turn to be a public health issue in Korea [1]. Since 2003, Korea has been the one of country with the highest suicide rate among 36 Organization for Economic Cooperation and Development (OECD) member [2]. The report of 2020 showed the 25.7 per 100,000 rate, which is more than twice the OECD average of 11.0 [3]. In addition, as the socioeconomic costs caused by suicide is higher than cerebrovascular disease or diabetes induced, it is not only an individual issue, but also an important social burden [4].

According to Psychological Autopsy Report in 2020 by the Korea Foundation for Suicide Prevention [5], 88.7% of people who completed suicide had suffered from a mental health disorder, and 81.7% had a depressive disorder. Therefore, assessing the risk of the suicide in depressive disorder patients will be crucial for suicide prevention. Suicidal ideation (SI) refers to thoughts or wishes to the ending one's own life. Previous studies have shown that 22.4−66% of major depressive disorder (MDD) patients had SI in the week before suicide [6-9]. In addition, one-third of individuals with SI were reported to be attempted suicide [10,11]. The literature reported that individuals with SI were four times more likely to commit suicide than one without SI [12]. Since SI is one of the strongest predictors of suicide [13], evaluating the SI in

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depressive disorder patients is expected to be a key for the intervention of suicide prevention. As such, higher SI in depressive disorder patients is consistently reported, a portion of patients have no SI even when the depression severity is severe [14]. Therefore, it is important to identify risk factors for SI in depressed patients. One of the factors is the impulsivity. A recent meta-analysis study of the relationship between impulsivity and suicide showed that there is a small but significant relationship between the two factors [15]. Anestis and Joiner [16] also insisted that the negative urgency (a facet of impulsivity) has the amplifier role between depressive states and SI. Furthermore, there was a report demonstrating that impulsivity has the predictive effect on suicidal proneness [17].

The previous studies on suicide risk and SI have been focusing the questionnaires, demographic information, and historical measures [18], but these information have the limitation of reliability and subjectivity. Therefore, there has been growing interest and efforts to find biomarkers that can objectively predict the risk of suicide [19]. Among various biomarkers, such as neurotransmitters and hormones [20,21], magnetic resonance imaging [22], the positron emission tomography [23], and electroencephalography (EEG), EEG has the advantage of being able to acquire relatively stable biological data at a relatively low cost. In addition, EEG is non-invasive, and data can be obtained with less discomfort to the subjects. Because of its non-invasiveness, relatively low cost, and excellent temporal resolution, EEG has advantages in discovering biomarkers related to human emotions and cognitive functions. In particular, event-related potential (ERP) has been the most popular biological methodology that can measure the high-level cognitive function of subjects undergoing EEG [24]. ERPs are derived from EEG data and reflect neural responses to specific, repeated events [25]. Because of the advantages as mentioned above and their potential clinical utility [26], ERPs have been widely used to study cognitive characteristics, including suicidal ideation and behaviors.

A representative ERP related to impulsivity especially on response inhibition is the ERP measured during the GoNogo task [27]. The GoNogo task consists of the presentation of a continuous series of "go" (i.e., the target) stimuli, to which participants are required to respond as accurately and quickly as possible, and "no-go" stimuli, which require participants to inhibit motor responses. Two major ERP components, Nogo-N2 and Nogo-P3 components are related to response inhibition. The Nogo-N2, a negative deflection can be observed between 200 and 300 ms after stimulus onset, has been suggested to reflect conflict monitoring [28,29]. The Nogo-P3, a large positive deflection can be observed between 300 and 600 ms after stimulus onset, has been proposed to reflect the inhibitory process itself [30,31]. There is a report that GoNogo ERP shows a decrease in amplitude in patients with borderline personality disorder who have difficulty in impulse control [32], and changes in antisocial personality disorder and attention-deficit/hyperactivity disorder (ADHD) have also reported [33,34]. As noted above, many researchers have focused the role of impulsivity in suicide, but there are a few studies examining the correlation between suicide and impulsivity through GoNogo ERP. In a recent study, a change in the N2 was reported in a group with a history of suicide attempt [35]. Another study reported that the suicide attempt group showed a decrease in Nogo-P3 amplitude compared to the suicide ideation group. However, there was no study of GoNogo ERP related to the suicidal ideation in depressive disorder patients.

We hypothesized that MDD patients with SI would exhibit significant differences in impulsivity relative to those without SI, and GoNogo ERP would reflect its differences. The purpose of this study is to identify the differences in Nogo ERP that reflects impulsivity between the MDD patients with and without suicidal ideation, and finally to determine the relation between impulsivity and SI. We also aimed to suggest the possibility of the ERP as a biomarker for impulsivity in MDD patients for evaluating suicidal ideation.

METHODS

Participants

This cross-sectional study enrolled 135 patients who were diagnosed with MDD and 27 healthy controls. Participants with MDD were recruited from July 2018 to June 2020 at the Psychiatry Department of Soonchunhyang University Seoul Hospital Korea. Patients with MDD were diagnosed by board-certified psychiatrists according to criteria of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) [36]. The participants were adults between 18 and 65 years of age. Patients who were unable to self-report due to head injury, neurological dis-

orders, or severe medical diseases and those who were diagnosed with a disorder other than MDD as the main diagnosis were excluded. All participants were right-handed. All participants completed a written consent in accordance with the Declaration of Helsinki. The study was approved by the Institutional Review Board of Soonchunhyang University Seoul Hospital (No. 2022-06-016-001).

Psychological Measures

To evaluate impulsivity severity, the Korean adult Attention Deficit Hyperactivity Disorder scale (K-AADHDS) was applied. The K-AADHDS is a scale originally developed by Murphy and Barkley [37] to measure ADHD symptoms in adults, and the Korean version was standardized by Kim [38]. This tool is a self-report questionnaire including 18 ADHD symptoms in DSM-IV, consisting of 9 items measuring inattention and the other 9 items measuring hyperactivity and impulsivity. We used 9 items to evaluate hyperactivity/impulsivity to measure the impulsivity severity of the participants. MDD patients who responded with a score of 3 or higher on five or more items were assigned to the high impulsivity group and the rest to the low impulsivity group [38].

We used Beck Scale for Suicidal ideation (SSI-BECK) to evaluate whether participants had suicidal ideation or not. The SSI-BECK is a self-report questionnaire developed by Beck *et al.* [39] to measure the severity of suicidal ideation. It is an important predictor of suicidal behavior and is highly correlated with clinicians' assessments of suicide risk [40]. The Korean version was standardized by Shin *et al.* [40] and well reflects the original questionnaire. The acceptable coefficient for Cronbach's alpha was 0.81. All patients with MDD were divided into SI group and without SI group based on their answers on items 4 (active suicidal ideation) or 5 (passive suicidal ideation) of the SSI-BECK.

The Beck Depression Inventory-II (BDI-II) was used to evaluate the severity of depressive symptoms. The BDI-II is a self-report questionnaire consisting of 21 items that measure current depressive symptoms. The Korean version of BDI-II was translated by Sung *et al.* [41], and the Cronbach's alpha was over 0.80. The Beck Anxiety Inventory (BAI) [42] was used to evaluate the participants' anxiety symptoms. The BAI is a self-report questionnaire comprising 21 questions measuring the severity of anxiety based on the importance of accurately distinguishing anxiety and depression. The BAI was translated into Korean by Kwon and Oei [42], and the Cronbach's alpha was 0.93 [43].

EEG Acquisition and Analyses

During the test, each participant was seated in a comfortable chair in a sound-attenuated EEG room at Soonchunhyang University Seoul Hospital. The EEG was acquired using a NeuroScan SynAmps amplifier (Compumedics USA) with 64 Ag-AgCl electrodes mounted on a Quik Cap using an extended 10−20 placement scheme. The ground electrode was located on a participant's forehead, and the physically linked reference electrodes were located at both mastoids. The vertical electrooculogram (EOG) was positioned above and below the left eye, and the horizontal EOG was recorded at the lateral canthus of each eye. The impedance was kept below 10 kΩ. All data were processed with a 0.1−70 Hz bandpass filter and sampled at 1,000 Hz. All subjects were asked to relax their entire body and sit comfortably without moving during the examination. They were able to look at the targets on the computer monitor screen comfortably without focusing while listening to the sound stimuli.

The recorded EEG data were preprocessed using CURRY 8 software. Gross artifacts, such as those caused by movements, were removed through visual inspection by a trained person with no prior information regarding the origin of the data. Artifacts related to eye movement or eye blinks were removed using the mathematical procedure implemented in the preprocessing software. The data were filtered using a 0.1−70 Hz bandpass filter and epoched from 100 ms pre-stimulus to 600 ms post-stimulus. The epochs were subtracted from the average value of the pre-stimulus interval for baseline correction. If any remaining epochs contained significant physiological artifacts (amplitude exceeding ± 75 μV) Vat any of the 62 electrode sites, they were excluded from further analyses. Only artifact-free epochs were averaged across trials and participants for ERP analyses.

Go/Nogo Experiment

Participants were seated comfortably in a silent test room. Stimuli for Go/Nogo task were presented acoustically through MDR-XB950N1 headphones (Sony). Two auditory stimuli, standard stimuli, and slightly higher-pitched target stimuli were used.

The subjects were instructed to press the spacebar as accurately and quickly as possible when the Go stimuli (low frequency, 1,000 Hz) were presented and not to respond when the Nogo stimuli (high frequency, 1,500 Hz) were. There were 400 trials, consisted of Go (85% probability) and Nogo (15% probability) conditions. The total examination time was about 12 minutes.

Following intervals for 700−1,000 ms, Go or Nogo targets were presented for 500 ms, and then, there was a interval for 1,500 ms before the next trial. These stimuli were generated by E-Prime software (Psychology Software Tools).

In the Nogo condition, the N2 (the most negative peak between 150 and 350 ms after stimulus onset) and the P3 (the most positive peak between 300 and 550 ms after stimulus onset) were investigated at the Fz, Cz, and Pz electrodes.

Statistical Analysis

To compare demographic and psychological characteristics among the MDD with SI group, without SI, and the control, analysis of variance (ANOVA) was performed. Tukey's test was used for the *post-hoc* analysis. Fisher's exact test was used for analyses of categorical variances. Analysis of Covariance (ANCOVA) was used with the age, sex, education, BDI-II and BAI scores as covariates to compare behavioral data, Go/Nogo ERP amplitudes and latencies with the Nogo condition at each electrode site (Fz, Cz, and Pz) between groups. Bonferroni test was used for the *post-hoc* analysis. To determine the differences in ERP according to the hyperactivity/impulsivity score of K-AADHDS, an independent t test was used for comparison between the high impulsivity group and low impulsivity group. In addition, the relationships between nogo ERP amplitudes and psychological scales were analyzed by Pearson's correlation. Statistical analyses were performed using SPSS 21 (IBM Co.).

RESULTS

Demographic and Psychological Characteristics

Table 1 shows the demographic and psychological characteristics of each group. MDD without SI group (45.1 ± 13.4) was significantly older than MDD with SI (35.8 ± 316.5, $p = 0.002$). The control group (28.89 ± 5.67) was younger than the MDD groups. There were no significant sex differences between groups ($p = 0.306$). In education level, the control group was more educated than MDD patients, but there was no difference between the MDD with SI and without SI groups. The MDD with SI group had significantly higher scores of Patient Health Questionnaire-9 (PHQ-9) ($p < 0.001$), BDI-II ($p < 0.001$), BAI ($p < 0.001$), and SSI-BECK ($p < 0.001$) compared to without SI or control groups.

Behavioral Data

Accuracy in Go trials showed significant differences between groups (Table 2). In the *post-hoc* test, MDD with

Table 1. Demographic and psychological characteristics of participants (n = 162)

Variable	Control (n = 27)	MDD without SI (n = 31)	MDD with SI (n = 104)	p value[a]	p value[b]
Age (yr)	28.89 ± 5.67	45.1 ± 13.4	35.8 ± 16.5	< 0.001	0.002
Sex					
Female	13 (48.2)	21 (67.7)	63 (60.6)	0.306	0.609
Male	14 (51.9)	10 (32.3)	41 (39.4)		
Education (yr)	16.07 ±1.62	13.71 ± 2.54	13.59 ± 3.31	0.003	0.849
K-AADHDS	21.93 ± 3.60	25.97 ± 7.77	35.01 ± 11.33	< 0.001	< 0.001
Hyperactivity/Impulsivity	10.56 ± 1.53	11.90 ± 3.85	16.04 ± 5.59	< 0.001	< 0.001
PHQ-9	2.33 ± 2.37	8.84 ± 6.70	17.3 ± 6.90	< 0.001	< 0.001
BAI	4.41 ± 5.08	26.45 ± 16.00	38.36 ± 15.42	< 0.001	< 0.001
BDI-II	4.04 ± 3.59	16.58 ± 11.18	33.9 ± 12.39	< 0.001	< 0.001
SSI-BECK	2.15 ± 3.55	2.16 ± 2.78	16.13 ± 8.89	< 0.001	< 0.001

Values are presented as mean ± standard deviation or number (%).
MDD, major depressive disorder; SI, suicidal ideation; ADHD, attention deficit hyperactivity disorder; K-AADHDS, Korean adult ADHD scale; PHQ-9, Patient Health Questionnaire-9; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II; SSI-BECK, Scale for Suicidal Ideation Beck; ANOVA, analysis of variance.
[a]Determined by use of One-way ANOVA for continuous variables and the Pearson χ^2 test for categorical variables. [b]Determined by *post-hoc* analysis between MDD group and MDD with suicidal ideation group using Turkey method.

Table 2. Comparison of behavioral data of GoNogo tasks between groups (n = 162)

Variable	Control (A)	MDD without SI (B)	MDD with SI (C)	p value[a]	*Post-hoc* p value[b]		
					A vs. B	A vs. C	B vs. C
Accuracy Go (%)	99.8 ± 0.28	98.9 ± 2.04	95.7 ± 7.61	0.007	1.000	0.162	0.017
Accuracy Nogo (%)	96.3 ± 2.84	96.2 ± 4.75	90.7 ± 12.00	0.017	1.000	0.648	0.019
False alarm rate (%)	3.7 ± 2.84	3.8 ± 4.75	9.3 ± 12.00	0.017	1.000	0.648	0.019
Reaction time (ms)	420.2 ± 66.00	501.7 ± 79.09	484.8 ± 97.78	0.042	0.115	0.041	1.000

All values are given as mean ± standard deviation values of participants.
MDD, major depressive disorder; SI, suicidal ideation; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II.
[a]p value is adjusted for age, sex, education, BDI-II and BAI. [b]Determined by Bonferroni test.

Table 3. Comparison of the amplitude of the Nogo N2 and P3 between groups (n = 162)

Amplitude	Control (A)	MDD without SI (B)	MDD with SI (C)	p value[a]	*Post-hoc* p value[b]		
					A vs. B	A vs. C	B vs. C
Nogo N2 Fz	−6.07 ± 6.09	−3.85 ± 5.20	−6.29 ± 5.02	0.260	1.000	1.000	0.319
Nogo P3 Fz	14.67 ± 6.72	12.53 ± 7.88	7.95 ± 5.72	0.001	0.407	0.002	0.013
Nogo N2 Cz	−4.92 ± 4.86	−2.87 ± 4.27	−4.1 ± 3.87	0.931	1.000	1.000	0.640
Nogo P3 Cz	15.94 ± 6.63	12.61 ± 7.13	9.55 ± 5.60	0.011	0.515	0.015	0.036
Nogo N2 Pz	−3.33 ± 3.51	−2.06 ± 3.35	−2.69 ± 2.86	0.675	1.000	1.000	1.000
Nogo P3 Pz	13.78 ± 6.63	10.45 ± 5.77	8.59 ± 4.87	0.015	0.235	0.013	0.276

All values are given as mean ± standard deviation values.
MDD, major depressive disorder; SI, suicidal ideation BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II.
[a]p value is adjusted for age, sex, education, BDI-II and BAI. [b]Determined by Bonferroni test.

SI group (95.7 ± 7.61) had significantly lower accuracy compared to MDD without SI (98.9 ± 2.04, p = 0.017). Both MDD with and without SI groups had no differences to control group (99.8 ± 0.28). Accuracy in Nogo trials also showed similar results. MDD with SI group (90.7 ± 12.00) showed significantly lower accuracy than in MDD without SI group (96.2 ± 4.75, p = 0.019). Both MDD groups with and without SI showed no difference to the control group (96.3 ± 2.84). Reversely, MDD with SI group showed the highest false alarm rate in the groups. MDD with SI group showed significantly longer reaction times compared to the control, but there is no difference between the MDD groups.

Comparison of Nogo ERP

The amplitude of Nogo ERP in each group is presented in Table 3 and Figure 1. Figure 2 shows the wave forms of Nogo ERP at each electrode. In the N2 amplitude, there were no significant differences observed between the groups in any electrodes.

In the P3 amplitude, all three electrodes had significantly differences between the groups (Fz; p = 0.001, Cz; p = 0.011, Pz; p = 0.015). The MDD with SI group had significantly decreased amplitudes compared to the controls in all electrodes of Fz, Cz, and Pz (p = 0.002, p = 0.015, and p = 0.013, respectively). On the other hand, the MDD without SI showed no significances compared to the controls. Compared to the MDD without SI, the MDD with SI group also showed significantly decreased amplitudes in Fz (p = 0.013) and Cz (p = 0.036), but not in Pz. Latencies of Nogo N2 and P3 had no significant differences between groups in all electrodes.

We also examined Nogo ERP differences between the high and low impulsivity groups according to K-AADHDS scores (Table 4). The high impulsivity group showed significantly lower P3 amplitudes than the low impulsivity group in Fz and Cz electrodes, but not in Pz. N2 amplitude did not differ between groups.

Correlation Analysis

Nogo P3 amplitudes at the Fz electrode had a significant correlation with hyperactivity/Impulsivity items of K-AADHDS, which coefficient was −0.35 ($p < 0.001$) (Fig. 3). Correlation with other psychological measures

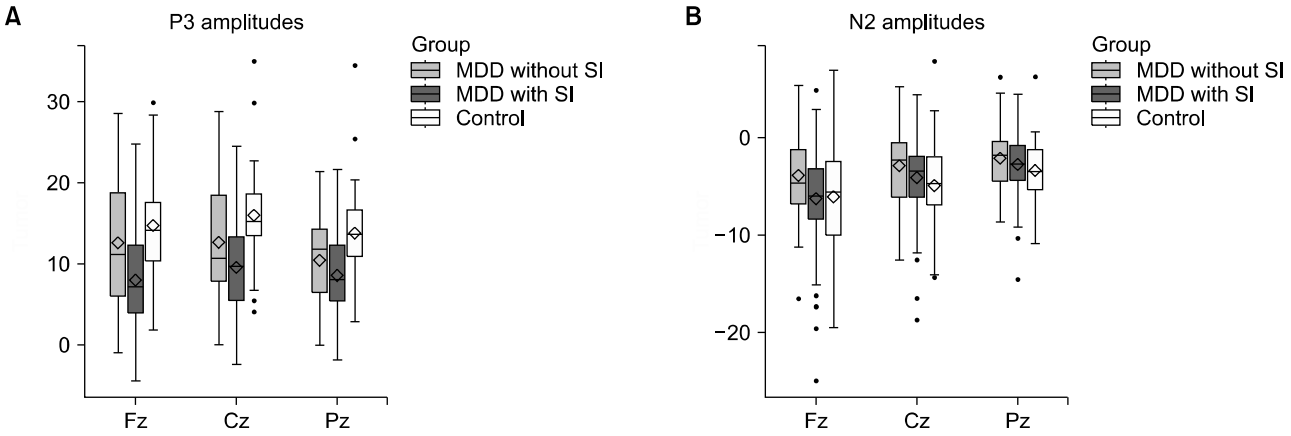

Fig. 1. Comparison of the amplitude of the Nogo N2 and P3 between groups (n = 162). The squares indicate mean of the scores. (A) P3 amplitude, (B) N2 amplitude.
MDD, major depressive disorder; SI, suicidal ideation.

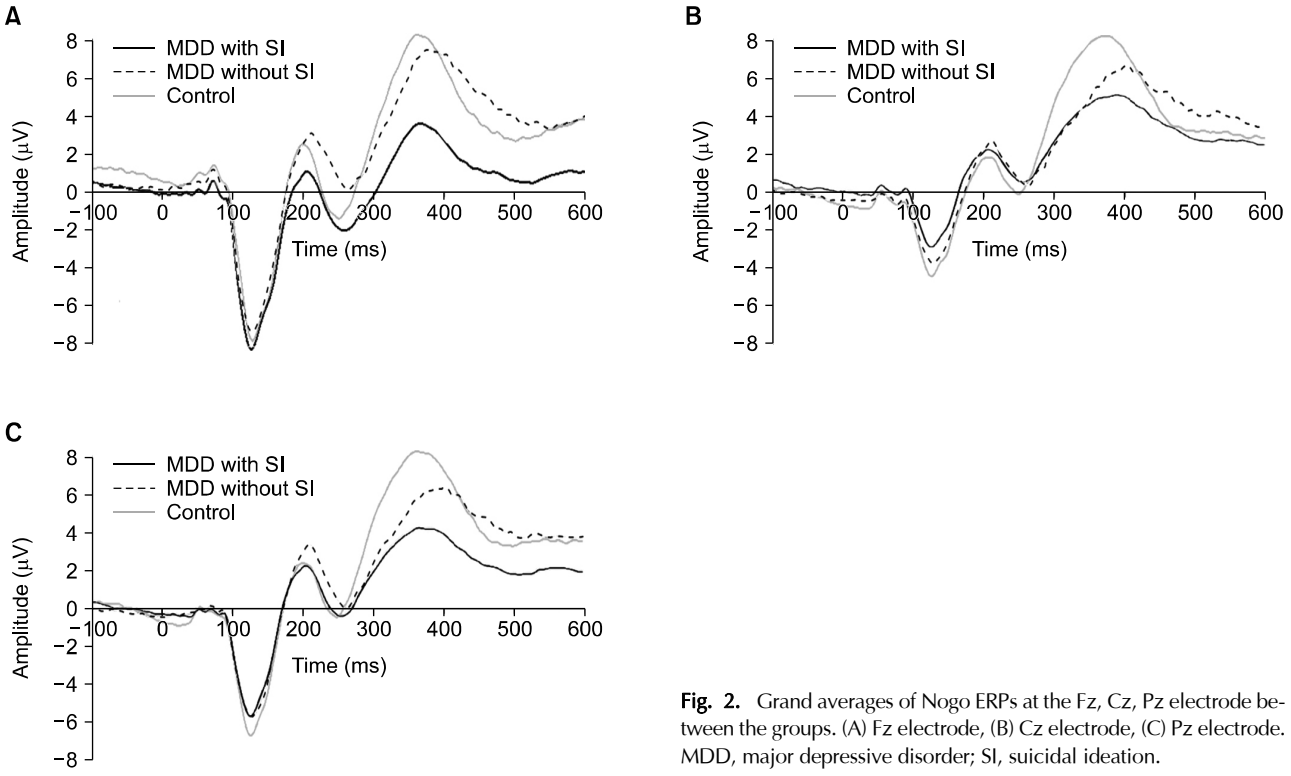

Fig. 2. Grand averages of Nogo ERPs at the Fz, Cz, Pz electrode between the groups. (A) Fz electrode, (B) Cz electrode, (C) Pz electrode.
MDD, major depressive disorder; SI, suicidal ideation.

and Nogo P3 amplitudes showed the significance, specifically BAI, BDI-II, SSI-BECK with -0.252 ($p = 0.001$), -0.289 ($p = 0.000$) and -0.281 ($p < 0.001$) of coefficient, respectively.

DISCUSSION

This study aimed to measure the impulsivity through Nogo ERP, which is widely known to be associated with response inhibition, and to observe the differences between MDD with SI and without group in purpose of determine the relation between impulsivity and suicidal ideation. As expected, Nogo P3 amplitude was significantly attenuated in the MDD with SI group compared to the MDD without or the control group.

First of all, we found that the impulsivity measured by

Table 4. Comparison of the amplitude of the Nogo N2 and P3 between high impulsivity and low impulsivity groups in MDD patients (n = 135)

Amplitude	Low impulsivity (n = 115)	High impulsivity (n = 20)	*p* value
Nogo N2 Fz	−5.73 ± 5.29	−5.72 ± 4.36	0.990
Nogo P3 Fz	9.61 ± 6.6	5.46 ± 5.02	0.003
Nogo N2 Cz	−3.83 ± 3.99	−3.77 ± 4.07	0.957
Nogo P3 Cz	10.86 ± 6.08	6.75 ± 5.00	0.003
Nogo N2 Pz	−2.59 ± 2.98	−2.33 ± 3.03	0.727
Nogo P3 Pz	9.37 ± 5.11	6.99 ± 4.87	0.055

All values are given as mean ± standard deviation values.
MDD, major depressive disorder.

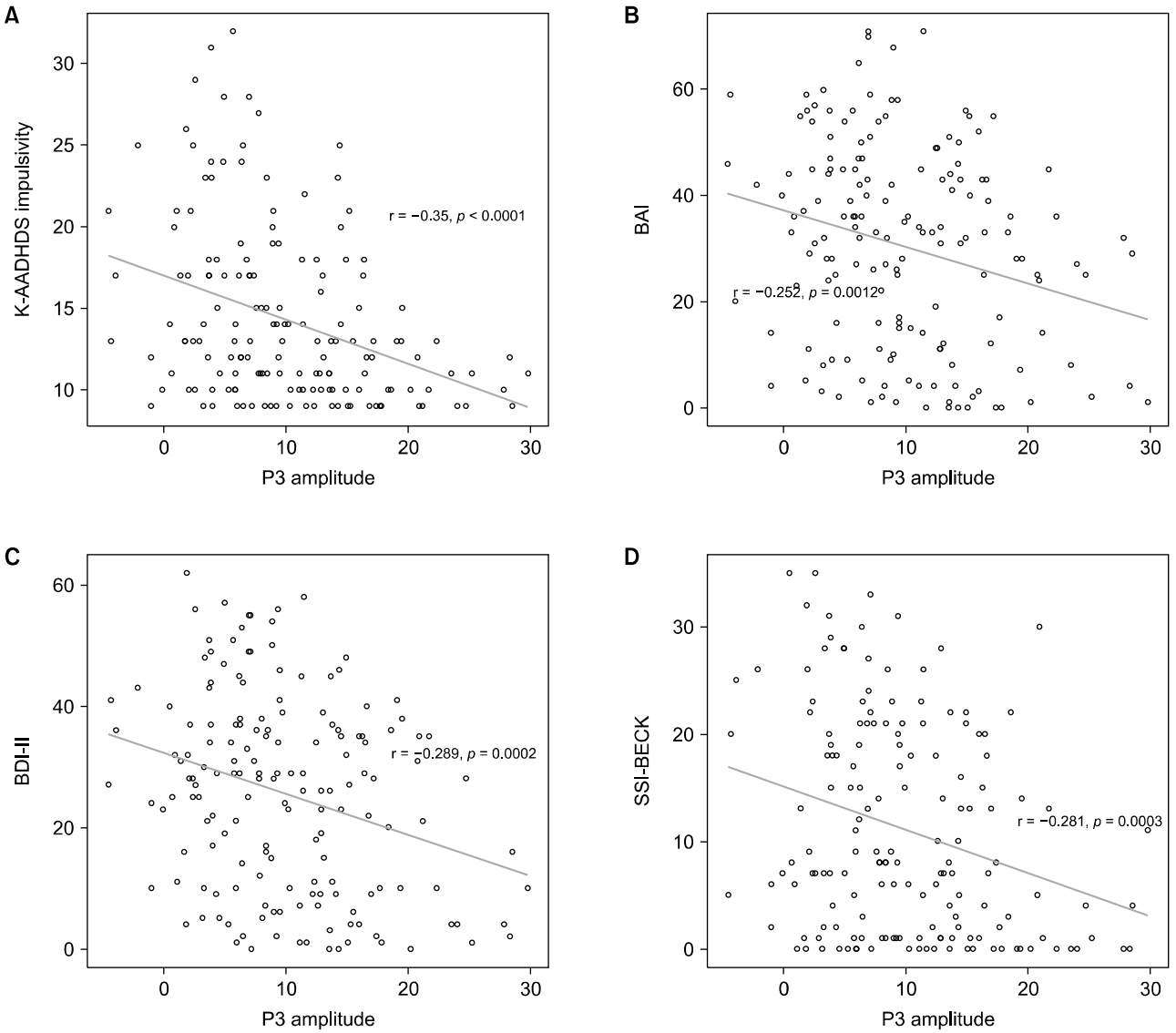

Fig. 3. Nogo P3 amplitude at Fz showed a significant correlation with (A) Korean adult Attention Deficit Hyperactivity Disorder Scale (K-AADHDS) Hyperactivity/Impulsivity, (B) Beck Anxiety Inventory (BAI), (C) Beck Depression Inventory-II (BDI-II), and (D) Scale for Suicidal Ideation Beck (SSI-BECK). (A) K-AADHDS Hyperactivity/Impulsivity; C = −0.35, $p < 0.001$. (B) BAI; C = −0.252, $p = 0.001$. (C) BDI-II; C = −0.289, $p < 0.001$. (D) SSI-BECK; C = −0.281, $p < 0.001$.

hyperactivity/impulsivity items of K-AADHDS were a significant higher in the MDD with SI group, compared to the MDD without SI groups. Furthermore, the behavioral data demonstrated that the false alarm rate in the MDD with SI was significantly higher than in the MDD without SI. False alaram rates and Nogo accuracy reflect motor-response inhibition [44,45]. Go Accuracy also showed similar results. The MDD with SI group showed significantly lower accuracy than MDD without SI group. The Go accuracy is known to reflect sustained and selective attention [46,47]. However, the reaction time, which also reflect also reflect sustained and selective attention [46,47], was not different between MDD with SI and without SI groups. The MDD with SI group only showed the longer reaction times compared to the control group. Collectively, MDD patients who have SI have higher impulsivity and poorer response inhibition than MDD patients who don't have SI and healthy subjects.

Considering the evidence from the previous studies showing Nogo ERP reflects the impulsivity [33,34,48], we expected that Nogo ERP could be distinguishable between the MDD with SI group and the without SI group. Our results included that MDD with SI group showed a significant decrease of Nogo P3 amplitude compared to the MDD without SI or the control group. Nogo P3 amplitude was also significantly attenuated in the high impulsivity group when compared to the low impulsivity group based on K-AADHDS scores. This is consistent with our precondition that the Nogo ERPs would reflect impulsivity and with the results of previous studies [27,30, 31]. Among the Nogo ERP, Nogo P3 components are related to the direct control response to inappropriate behavior during the response inhibition process [49,50]. In addition, it is considered that P3 reflects higher cognitive function devoted to response inhibition, so the amplitude of P3 while performing the Nogo task was implies to be the cognitive resources that the subject can be used in impulse control [51]. Therefore, this result indicates that the cognitive ability to control response inhibition declined in the MDD with SI than in the MDD without SI, suggesting that the MDD with SI has poor ability to response inhibition.

The recent studies highlighted the relationship between depression, impulsivity, and suicidal ideation [52-54]. Wang *et al.* [53] indicated that impulsivity has moderating effect on the relationship between depression severity and SI. The study stated that patients with higher impulsivity are more likely to have suicidal ideation even when they are less depressed than patients with low impulsivity [53]. In addition, Zhang *et al.* [54] also suggest that impulsiveness could indirectly lead to suicidal ideation through depression and enhance the indirect effect. They insisted that people who have impulsive traits are more likely to have suicidal ideation because they have more suffering from depression [54]. Our results demonstrated that the MDD without SI group had no differences of Nogo ERP compared to the control, but the MDD with SI had significantly attenuated Nogo P3 amplitude, which support these hypotheses.

Another study about brain structural changes related to the suicidal ideation in patients with depression found that the gray matter volumes (GMV) of the right and left dorsolateral prefrontal cortex (DLPFC) and right ventrolateral prefrontal cortex (VLPFC) are decreased in the MDD with SI compared to without SI and healthy controls (HC) [55]. The MDD without SI group only exhibited significant decrease in the left DLPFC relative to the HC group, but not in the right DLPFC or right VLPFC [55]. The findings suggest that the decrease in the GMVs of right DLPFC and right VLPFC is related to suicidal ideation rather than MDD condition and left DLPFC reductions were associated with both MDD and SI. The one of the roles of the right VLPFC is response inhibition [56]. This is consistent with our results that the MDD with SI group had significant decreases in response inhibition compared to the MDD without SI group and the control group, but the MDD without SI group had no differences from the control group. These results are likely related to the structural changes in the brain which pointed out in the study that we discussed above [55]. As our study did not examine the association between ERP and structural changes in the brain, it will need to be confirmed in future studies.

Nogo N2 component did not show any significant differences between the groups. There were controversial results of Nogo N2 component differences between suicidal attempters and suicidal ideators in the previous studies [35,57]. Albanese *et al.* [35] reported that the suicidal attempters had the more positive N2 amplitude than suicidal ideators. On the contrary, Yoon *et al.* [57] reported no differences of Nogo N2 ERP. To our knowledge, none of studies have investigated the differences of Nogo N2 ERP in condition with the presence or absence of SI in MDD

patients. Nogo N2 ERP is known to be related to conflict itself or the consequences of a conflict, such as inhibition or revision of inappropriate response tendencies [58]. In addition, Nogo N2 is sensitive to manipulations of stimulus frequency [59]. On the other hand, Ruchsow *et al*. insisted that the Nogo N2 amplitude is possibly more related to compulsivity than impulsivity in a Go/Nogo study in the obsessive-compulsive patients [60]. As studies on suicidality and Nogo N2 are limited, the further studies in other subjects are necessary in the future.

In correlation analysis, Nogo P3 amplitude in the Fz electrode showed a significant negative correlation with hyperactivity/impulsivity items of K-AADHDS. The higher the impulsivity is, the lower the amplitude of Nogo P3 was shown. There were also significant negative correlations between Nogo-P3 amplitude and depression (BDI-II) and its amplitude with suicidal ideation (SSI-BECK) scores. These results suggest that when the impulsivity increases, the depression severity and SI also get severe. This findings is consistent with the studies stated above [52-54], on the relationship between depression, impulsivity, and SI. The inter-relationship between each variables should be explored in further studies.

There are some limitations in the current study. First, the sample size was relatively small, especially in MDD without SI and the control group. It is necessary to confirm the results by conducting with a larger number of participants in the future. Second, the effect of smoking could not be excluded. Smoking is known to be related to the neurotransmission of dopamine and serotonin and there is a possibility of its affects to the P3 amplitude slope. Therefore, the effect of smoking should be evaluated in the future. Third, although subjects were diagnosed with MDD by an experienced psychiatrist at the time of enrollment and patients with bipolar disorder were excluded, we could not exclude subsequent re-diagnoses of bipolar depression. Finally, other factors that also could affect ERP components such as psychiatric drug history, past history of suicidal behaviors and lifetime psychiatric diagnosis were not considered [61-63]. Further studies should consider these factors to compensate this limitation.

In this study, we confirmed that the Nogo P3 ERP amplitude was reduced in MDD patients with suicidal ideation compared to MDD without suicidal ideation and controls. Nogo-P3 ERP reflects the impulsivity, which contributes to suicidal ideation. Thus, we suggest Nogo ERP is a non-invasive and economical tool for measuring the impulsivity related to suicidal ideation and it is a candidate for a biomarker of suicide risk in patients with major depression. Through future studies that supplement the limitations of this study, Nogo-ERP is expected to contribute to decrease the suicide rate by evaluating and predicting the suicide risk of depressed patients.

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■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Minjae Kim, Yeon Jung Lee. Data acquisition: Minjae Kim, Yeon Jung Lee, Jaeuk Hwang, Sung-il Woo, Sang-Woo Hahn. Formal analysis: Minjae Kim, Yeon Jung Lee. Funding: Yeon Jung Lee. Supervision: Jaeuk Hwang, Sung-il Woo, Sang-Woo Hahn. Writing—original draft: Minjae Kim. Writing—review & editing: Minjae Kim, Yeon Jung Lee, Sang-Woo Hahn.

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