






Neural correlates of reward valuation in individuals with nonsuicidal self-injury under uncertainty

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Original Article

Cite this article: Lee JO, Moon H, Zoh S-M, Jo E, Hur J-W (2024). Neural correlates of reward valuation in individuals with nonsuicidal self-injury under uncertainty. *Psychological Medicine* **54**, 3251–3260. <https://doi.org/10.1017/S0033291724001363>

Received: 7 October 2023

Revised: 5 February 2024

Accepted: 10 May 2024

First published online: 6 September 2024

Keywords:

decision-making; emotion regulation; fMRI; hippocampus; middle cingulate cortex; nonsuicidal self-injury; uncertainty

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Abstract

Background. Attitudes toward risk and ambiguity significantly influence how individuals assess and value rewards. This fMRI study examines the reward valuation process under conditions of uncertainty and investigates the associated neural mechanisms in individuals who engage in nonsuicidal self-injury (NSSI) as a coping mechanism for psychological pain.

Methods. The study involved 44 unmedicated individuals who reported five or more NSSI episodes in the past year, along with 42 age-, sex-, handedness-, IQ-, and socioeconomic status-matched controls. During the fMRI scans, all participants were presented with decision-making scenarios involving uncertainty, both in terms of risk (known probabilities) and ambiguity (unknown probabilities).

Results. In the NSSI group, greater attitudes toward ambiguity were correlated with increased emotion reactivity and adverse method versatility. Whole-brain analysis revealed notable group-by-condition interactions in the right middle cingulate cortex and left hippocampus. Specifically, the NSSI group showed decreased neural activation under ambiguity *v.* risk compared to the control group. Moreover, reduced hippocampal activation under ambiguity in the NSSI group was associated with increased emotion regulation problems.

Conclusions. This study presents the first evidence of reduced brain activity in specific regions during value-based decision-making under conditions of ambiguity in individuals with NSSI. These findings have important clinical implications, particularly concerning emotion dysregulation in this population. This study indicates the need for interventions that support and guide individuals with NSSI to promote adaptive decision-making in the face of ambiguous uncertainty.

Nonsuicidal self-injury (NSSI) refers to deliberate, self-inflicted damage to body tissues without suicidal intent (International Society for the Study of Self-Injury [ISSI], 2018). NSSI has become a concern due to its high prevalence, affecting up to 22.0% of adolescents (Xiao, Song, Huang, Hou, & Huang, 2022) and 13.4% of young adults (Swannell, Martin, Page, Hasking, & St John, 2014). Understanding why some individuals choose to engage in physical self-harm to cope with psychological distress is a central challenge in the study of NSSI (Hooley & Franklin, 2018; Lee, Shin, Kim, Moon, & Hur, 2023). To date, our comprehension of the decision-making processes in individuals with NSSI and their underlying pathophysiological mechanisms remains limited, thereby impeding an integrative understanding of NSSI (Kaess et al., 2021).

Individuals' decisions to engage in self-injury contradict the intrinsic drive for self-preservation (Nock, 2010). However, NSSI, which may cause significant long-term distress, may be an appealing coping strategy for some individuals owing to its apparent short-term benefits (Bresin, 2020). Recent literature reviews suggest that individuals who engage in NSSI exhibit an aberrant decision-making process with respect to weighing the probabilities and outcomes of the available options for reward (Bettis et al., 2022; Kaess et al., 2021; Schreiner, Klimes-Dougan, Begnel, & Cullen, 2015), thereby promoting research on reward valuation in NSSI.

Weaknesses in the ability to predict and make decisions under uncertainty have been linked to the development and exacerbation of psychopathology (Hasler, 2012; Hélie, Shamloo, Novak, & Foti, 2017). Aberrant value-based decision-making processes under uncertainty have been linked to various mental health conditions (Cuthbert, 2022; Nguyen et al., 2019), including posttraumatic stress disorder (Ruderman et al., 2016), major depressive disorder (Mukherjee, Lee, Kazinka, Satterthwaite, & Kable, 2020), suicide attempts (Alacreu-Crespo et al., 2020; Deisenhammer, Schmid, Kemmler, Moser, & Delazer, 2018), and behavioral addictions such as pathological gambling (Brevers et al., 2012, 2015). Given the pivotal role of emotion in reward valuation under uncertainty (Loewenstein, Weber, Hsee, & Welch, 2001; Paulus & Angela, 2012; Ruppel, Stankevicius, Huys, Series, & Steele, 2021) and of emotion regulation in NSSI pathology (McKenzie & Gross, 2014; Taylor et al., 2018;

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Wolff et al., 2019), it is important to investigate reward valuation in NSSI. However, owing to the lack of research in this area, no empirical evidence exists on altered reward valuation in NSSI (Bettis et al., 2022). Therefore, this study aimed to elucidate the neurobiological mechanisms involved in reward valuation processes of individuals with NSSI, particularly under uncertain conditions (Glimcher & Rustichini, 2004). In this study, we hypothesized that individuals with NSSI would exhibit deviated activation in brain regions during reward valuation under uncertainty relative to controls. These regions were expected to include the orbitofrontal cortex (OFC), a central region for emotion regulation and reward valuation (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001), and the middle cingulate cortex (MCC), a region proposed to mitigate uncertainty-induced conflict (Grupe & Nitschke, 2013).

In addition, given that recent neuroeconomic research investigating value-based decision-making has distinguished uncertainty into risk and ambiguity with known and unknown probabilities, respectively (Wu, Sun, Camilleri, Eickhoff, & Yu, 2021), we sought to identify the characteristics of value-based decision-making under risk and ambiguity in individuals with NSSI. Various psychopathological studies have identified dissociable behavioral and neural patterns of reward valuation under risk and ambiguity (Fujino et al., 2016, 2017; Pushkarskaya et al., 2015; Ruderman et al., 2016). Furthermore, we expected to observe aberrant activation in the prefrontal areas, inferior parietal gyrus, and anterior insula, which are known to be recruited more in value-based decision-making under ambiguity compared to risk (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005; Huettel, Stowe, Gordon, Warner, & Platt, 2006; Levy, Snell, Nelson, Rustichini, & Glimcher, 2010), because the ambiguity condition with unknown probabilities places greater mental demands on individuals compared to the risk condition with known probabilities (FeldmanHall, Glimcher, Baker, & Phelps, 2016).

In summary, the primary goal of this study was to investigate value-based decision-making and its neural correlates in individuals with NSSI under uncertainty. Although altered OFC activation has been observed during reward processing in those with NSSI (Sauder, Derbidge, & Beauchaine, 2016; Vega et al., 2018), no study has directly compared the neural properties associated with their reward valuation under risk and ambiguity. More importantly, this study sought to advance our understanding of the complex nature of NSSI pathology by more precisely defining the uncertainties (i.e. risk *v.* ambiguity) to which individuals with NSSI are vulnerable and examining how these environmental contexts relate to their emotional processing problems.

Methods

Participants and procedures

From August 2021 to September 2022, 99 potential participants aged between 19 and 29 years were recruited through public online advertisements. After verbal consent was obtained, all study candidates underwent an initial telephone screening to ensure their eligibility for the study (i.e. demographic information; NSSI behaviors; history of medical, psychiatric, and neurological conditions; and presence of MRI contraindications). Prospective participants who were not excluded during the initial screening were then invited to an in-person or videoconferencing interview, where they completed the Structured Clinical Interview for DSM-5 disorders (SCID-5) (First, 2014). These semi-

structured interviews, including the SCID-5, were conducted by well-trained clinical graduate students under the supervision of two licensed clinical psychologists.

Fifty-two individuals who reported five or more NSSI episodes in the past year were included in the NSSI group. The Inventory of Statements about Self-Injury (ISAS) (Glenn & Klonsky, 2009; Kim, Kim, & Hur, 2019) was used to assess the frequency, function, and method versatility of NSSI. Participants who only reported skin-picking, hair-pulling, or nail-biting as a method of NSSI were excluded, given the proposed diagnostic criteria for NSSI in the DSM-5. Forty-seven individuals with no history of NSSI behaviors and no diagnosis of psychiatric disorders were recruited as controls. The NSSI and control groups were matched for age, sex, handedness, IQ, education, and socioeconomic status.

The exclusion criteria for both groups were as follows: (1) any history of neurological or psychotic disorders, (2) use of psychotropic medication or participation in psychotherapy in the past month, (3) an estimated IQ below 80 on a short form of the Korean version of the Wechsler Intelligence Scale (K-WAIS) (Choe et al., 2014; Wechsler, 2008), and (4) ineligibility for MRI. Additionally, as suggested by previous studies on ambiguity aversion (Brevers et al., 2012, 2015; Buckholtz, Karmarkar, Ye, Brennan, & Baskin-Sommers, 2017), individuals diagnosed with gambling or antisocial personality disorders were excluded from the study.

Participants with technical problems (1 NSSI, 1 control), drowsiness or dizziness (3 NSSIs, 3 controls), abnormal MRI findings (1 NSSI, 1 control), non-fluent Korean speakers (1 control), or inaccurate performance via randomly pressing buttons (2 NSSIs) were excluded from the analysis. No participants were excluded because of excessive head movements. Therefore, 44 individuals with NSSI and 42 controls were included in the final sample. Written informed consent was obtained from all the participants, and the study protocol was approved by the Institutional Review Board of Korea University (IRB No. KUIRB-2021-0144-09).

Measures

Intolerance to Uncertainty Scale-12 (IUS-12)

The IUS-12 (Carleton, Norton, & Asmundson, 2007) is a 12-item abbreviated version of the original 27-item IUS (Freeston, Rhéaume, Letarte, Dugas, & Ladouceur, 1994), a transdiagnostic assessment tool for trait IU. Items on the IUS-12 assess general reactions to uncertainty, ambiguous situations, and upcoming events using a 5-point Likert scale. The IUS-12 has been shown to have two factors: (1) prospective anxiety and (2) inhibitory anxiety. Higher scores indicate higher IU levels. In this study, the IUS-12 demonstrated excellent internal consistency ($\alpha = 0.93$).

Emotion Reactivity Scale (ERS)

The ERS is a 21-item scale that measures emotion reactivity, consisting of sensitivity, intensity, and persistence of emotions (Nock, Wedig, Holmberg, & Hooley, 2008). The ERS has a high internal consistency of 0.94. Each item is scored on a 5-point Likert scale ranging from 0 to 4. The higher the total ERS score, the higher the level of emotion reactivity. Cronbach's α for the current study was 0.97.

Difficulties in Emotion Regulation Scale (DERS)

The DERS is a 36-item self-report measure of emotion regulation on a scale of 1–5 (Gratz & Roemer, 2004). The DERS has six factors: (1) impulse control difficulties, (2) lack of attention to and awareness of emotions, (3) non-acceptance of emotions, (4) lack of emotional clarity, (5) limited access to emotion regulation strategies, and (6) difficulties in engaging in goal-directed behavior. Higher DERS scores indicate greater levels of emotion dysregulation. Item 17 showed a negative loading on the factor analysis of the Korean version of the DERS (Cho, 2007) and was therefore excluded from the scoring. The DERS yielded an excellent internal consistency of 0.98 in the current sample.

fMRI task: the Ellsberg paradox task

The Ellsberg paradox task (Fig. 1) comprises 60 monetary decision-making trials. Participants were required to respond to forced-choice items by pressing a button indicating whether to choose a *reference* option (50% chance of winning \$16), which remained the same in every trial, or a *variable* option in which lottery details were systematically manipulated. The resulting probabilities were visualized in boxes containing 24 balls colored either red (winning color) or blue (losing color). Participants were informed that the picture conveyed information about the amount and probability of winning, and that they would be rewarded based on the outcome of the ball they selected from the two lotteries.

In half of the trials where the entire box was visible, the exact ratio of red to blue balls was displayed, providing participants with the necessary information for their reward valuation (referred to as the ‘known probability,’ i.e. ‘risk’ condition). In the other half of the lottery trials, part of the box was obscured by a gray occluder so that the probability of the outcome was only partially visible (referred to as the ‘unknown probability,’ i.e. ‘ambiguity’ condition).

Six different winning probabilities (0.125, 0.25, 0.375, 0.625, 0.75, and 0.875) were used in the risky condition, and three different occluder sizes (covering 25, 50, or 75% of the box) were used in the ambiguous condition. Increasing the size of the occluder increases the level of ambiguity. Each lottery option was \$12, \$16, \$24, \$40, or \$80. The amounts of each lottery option varied slightly (\pm \$ 0.8) across trials to prevent participants from developing automatic responses. Each trial began with a 720 ms white fixation cross and was presented in a randomized order, yielding a total of 60 choices ($[6 \text{ probabilities} \times 5 \text{ amounts}] + 2 \times [3 \text{ ambiguity levels}] \times [5 \text{ amounts}]$). Participants had to respond within 230 ms. After completing practice trials to ensure comprehension of the task, we did not provide feedback to participants during the fMRI scan to prevent influencing their performance. We also avoided using the terms ‘risky’ and ‘ambiguous’ with participants during the experiment.

In accordance with established research procedures (Smith & Smith, 1991; Xu et al., 2016), participants were offered monetary incentives for task performance based on the distribution of accumulated rewards in the pilot trial, in addition to the show-up fee. All participants were informed that the accumulated rewards would be used to provide real monetary incentives.

MRI protocols and image acquisition

Data were acquired using a MAGNETOM Trio 3 T scanner with a 32-channel head coil (Siemens, Erlangen, Germany) at Seoul National University. Functional scans were acquired using a T2*-weighted gradient-echo planar imaging (EPI) sequence (TR = 2400 ms; TE = 30 ms; FOV = 192 × 192 mm; flip angle = 90°; voxel size = 3.0 mm³). Forty interleaved axial slices parallel to the anterior-posterior commissure plane were collected. A total of 241 volumes were obtained in a run of 583 s for each participant, with the first two EPI volumes of non-steady-state data being discarded. High-resolution T1-weighted structural scans (TR = 2400 ms; TE = 2.19 ms; FOV = 272 × 272 mm; flip angle = 8°; voxel size = 0.8 mm³) were acquired for each participant.

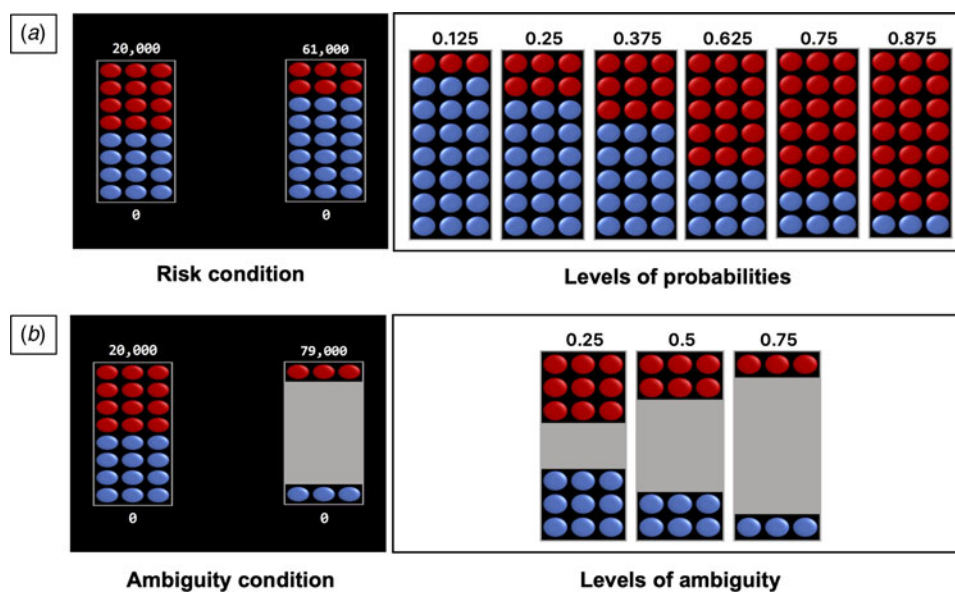


Figure 1. Experimental paradigm. Participants responded to the forced-choice items by choosing either a reference option (50% chance of winning \$16) or a variable option in which the lottery details were systematically manipulated. (a) In the risk condition, the exact ratio of red to blue balls was displayed. The levels of probabilities were varied within the condition. (b) In the ambiguity condition, the probability of the outcome was only partially visible at different levels of ambiguity. Six different winning amounts on a variable option payoffs were used in both conditions (\$12, \$16, \$24, \$40, or \$80).

During scanning, foam padding was used to minimize head motion, and an eye tracker was incorporated to ensure the participants' alertness.

Data analysis

Behavioral data

Attitudes under risk and ambiguity were estimated based on participants' choice between the two lotteries, as per the methodology described by Fujino et al. (2016). In the risk condition, participants were asked to choose between a high probability of receiving a low reward and a low probability of receiving a high reward. Risk aversion refers to the inclination to avoid the latter, even if its expected value is higher than that of the former (Levy et al., 2010). The measure of risk aversion was obtained by comparing the rate of [risk-averse choice – risk-seeking choice], with higher values indicating higher levels of risk aversion.

For the ambiguity condition, participants were asked to choose between a lottery of known probability and a lottery of unknown probability (i.e. concealed behind an occluder). Ambiguity aversion refers to the inclination to avoid the latter (Ellsberg, 1961). Ambiguity attitudes were obtained by comparing the rate of [ambiguity-averse choice – ambiguity-seeking choice], with higher values indicating greater levels of ambiguity aversion. We also conducted a mixed analysis of variance (mixed ANOVA) to compare choice preferences according to the level of each condition.

Additionally, we examined the rate at which each participant selected the lottery with a lower amount and probability. Participants who preferred the inferior option more than 50% of the time were excluded from the analysis, as this behavior was interpreted as random button pressing rather than a deliberate decision-making process.

fMRI data: A standard preprocessing pipeline was implemented using the CONN toolbox (version 21. a) (Whitfield-Gabrieli & Nieto-Castanon, 2012) using the MATLAB software (MathWorks, Natick, MA, USA). The pipeline included realignment and unwarping to correct for motion artifacts, correction of slice timing, segmentation of the brain tissue into gray matter, white matter, and cerebrospinal fluid, normalization to a standard template, and spatial smoothing using a Gaussian kernel with a 6-mm full-width half-maximum (FWHM). Six motion regressors were also included to minimize the confounding effects of head motion.

For the first-level analysis, a general linear model (GLM) analysis was performed using Statistical Parametric Mapping (SPM) 12 (Wellcome Trust Center for Neuroimaging, London, UK). The two task conditions (risk and ambiguity) were modeled as predictors at the individual level, and the contrasts of ambiguity > risk and risk > ambiguity were used for the group-level analysis. A full factorial design analysis (whole-brain analysis) included the main effects of group and condition as well as group-by-condition interactions. A two-sample *t* test was used as a post-hoc test. In this study, results were reported as significant if they survived family-wise error (FWE) correction with a threshold of $p < 0.05$. A threshold of $p < 0.005$ (uncorrected and $k > 40$) was used for exploratory analyses.

The MarsBaR toolbox (Brett, Anton, Valabregue, & Poline, 2002) was used to extract task-related mean parameter estimates (beta values) from clusters of significant group-by-condition interactions. We then used Pearson's correlation to examine the associations between the variables of interest in the NSSI group. The Bonferroni correction was applied to correct for multiple comparisons, and $p < 0.017$ was considered significant ($0.05/3 = 0.017$). All statistical analyses were performed using Jamovi version 2.3.

Results

Sociodemographic and clinical characteristics

The NSSI and control groups did not differ in age, sex, socioeconomic status, educational level, estimated IQ, or handedness (all p s > 0.05). Regarding clinical characteristics, there were significant differences in the IUS, ERS, and DERS scores ($t_{(83)} = 5.66$, $p < 0.001$; $t_{(83)} = 7.80$, $p < 0.001$; $t_{(83)} = 8.32$, respectively). Sociodemographic and clinical characteristics are summarized in Table 1.

Behavioral data

Reaction time in risk v. ambiguity

For reaction times, the main effect of the condition was statistically significant ($F_{(1, 84)} = 70.89$, $p < 0.001$, $\eta_p^2 = 0.46$), indicating that the reaction times were longer in the ambiguity condition than in the risk condition. However, neither the main effect of group nor the interaction between group and condition was significant ($F_{(1, 84)} = 0.16$, $p = 0.69$; $F_{(1, 84)} = 0.97$, $p = 0.33$, respectively).

Attitudes under risk and ambiguity

The attitude scores in risk and ambiguity conditions did not differ significantly between groups ($t_{(84)} = 0.89$, $p = 0.38$; $t_{(84)} = -0.06$, $p = 0.95$). In further analysis, the 2 (group) \times 5 (amounts of winning) mixed ANOVA revealed a significant main effect of the winning amounts ($F_{(4, 336)} = 236.84$, $p < 0.001$, $\eta_p^2 = 0.74$), indicating that participants were more likely to choose the lottery with higher expected value. However, neither the main effect of group nor the interaction between group and amount of winnings was statistically significant ($F_{(1, 84)} = 0.18$, $p = 0.67$; $F_{(4, 336)} = 1.23$, $p = 0.30$, respectively).

A two (group) \times 6 (probabilities of winning) mixed ANOVA revealed that both the main effect of probabilities and the group-by-probabilities interaction were significant ($F_{(5, 420)} = 675.23$, $p < 0.001$, $\eta_p^2 = 0.89$; $F_{(5, 420)} = 2.25$, $p = 0.049$, $\eta_p^2 = 0.03$, respectively), whereas no significant main effect of group was observed ($F_{(1, 84)} = 1.39$, $p = 0.24$).

In addition, both groups were significantly less likely to choose lotteries with occluder compared to lotteries without occluder as the levels of ambiguity increased ($F_{(2, 168)} = 100.36$, $p < 0.001$, $\eta_p^2 = 0.54$). However, we did not find a main effect of group or an interaction between group and ambiguity level ($F_{(1, 84)} = 0$, $p = 0.99$; $F_{(2, 168)} = 2.25$, $p = 0.10$, respectively).

Correlation analysis between behavioral and clinical features

In the NSSI group, the scores for aversive attitudes under risk were not statistically related to clinical characteristics. In contrast, the scores for aversive attitudes under ambiguity were positively correlated with emotion reactivity ($r = 0.41$, $p = 0.006$) and NSSI versatility ($r = 0.42$, $p = 0.005$).

fMRI data

Whole-brain full-factorial ANOVA during valuation of uncertain options

The results of the full-factorial design analysis are summarized in Table 2. Significant main effects of group were observed in the right superior frontal gyrus, right precentral gyrus, OFC, left fusiform gyrus, and bilateral occipital lobe ($p < 0.005$, uncorrected). A significant main effect of condition was found in the left OFC, right superior frontal gyrus, left precuneus, right inferior parietal

Table 1. Demographic and clinical data of the included participants

	NSSI (<i>n</i> = 44)	Control (<i>n</i> = 42)	<i>t</i> or χ^2	<i>p</i>
Age (years)	21.2 ± 2.0	22.1 ± 2.6	1.88	0.063
Sex (female/male)	37/7	35/7	0.91	0.341
Socioeconomic status			7.33	0.119
Low	1 (2%)	1 (2%)		
Moderate-low	9 (21%)	2 (5%)		
Moderate	15 (35%)	14 (33%)		
Moderate-high	14 (33%)	23 (55%)		
High	4 (9%)	2 (5%)		
Educational level			1.08	0.582
Some college or university	38 (86%)	33 (79%)		
College or university graduate	4 (9%)	5 (12%)		
Some graduate school or more	2 (5%)	4 (10%)		
Estimated IQ	105.70 ± 10.09	106.31 ± 9.58	0.29	0.775
Handedness (right/left)	40/4	40/2	0.62	0.431
NSSI versatility ^a	4.88 ± 2.40			
Suicide attempt (past 12 months)	10 (23%)			
Comorbid psychiatric diagnosis	26 (59%)			
IUS	37.12 ± 9.49	25.60 ± 9.25	5.66	< 0.001
ERS	43.23 ± 18.87	14.44 ± 14.72	7.80	< 0.001
DERS	109.26 ± 28.56	63.95 ± 20.98	8.32	< 0.001
Reaction time on fMRI task (ms)				
Risk	1.17 ± 0.19	1.17 ± 0.17	−0.13	0.894
Ambiguity	1.25 ± 0.20	1.28 ± 0.20	−0.62	0.538
Attitude score on fMRI task				
Risk	0.47 ± 0.37	0.40 ± 0.34	0.89	0.375
Ambiguity	0.50 ± 0.23	0.51 ± 0.24	−0.06	0.949

Notes. NSSI, nonsuicidal self-injury; IUS, Intolerance to Uncertainty Scale; ERS, Emotion Reactivity Scale; DERS, Difficulties in Emotion Regulation Scale.

^aThe number of NSSI methods used.

gyrus, left supramarginal gyrus, and left occipital lobe ($p < 0.05$, FWE-corrected). Notably, significant group-by-condition interactions were identified in the right MCC and left hippocampus, resulting from decreased activation in the NSSI group compared to the control group during value-based choice processes under ambiguity *v.* risk (Fig. 2).

Correlations between fMRI activation and clinical measures within the NSSI group

The hippocampus hypoactivation, which showed decreased activation in the NSSI group under ambiguity *v.* risk contrast, was associated with increased difficulty in emotion regulation within the NSSI group ($r = -0.41$, $p = 0.006$) (Fig. 3). In the control group, we found no significant correlations between brain activation and clinical variables.

Discussion

To the best of our knowledge, this is the first study to examine the neural mechanisms involved in making value-based choices in

individuals with NSSI. This study found significant group effects in frontal brain areas, including the left OFC, superior frontal gyrus, and precentral gyrus. Our findings align with prior research on pain-processing aspects of NSSI, suggesting a link between NSSI and aberrant activation in brain regions responsible for cognitive reward processing (Osuch, Ford, Wrath, Bartha, & Neufeld, 2014). More importantly, our findings revealed significant group-by-condition interactions in the right MCC and left hippocampus. This was attributed to decreased neural activation in the NSSI group compared to controls during reward valuation under ambiguity *v.* risk. Furthermore, the reduced hippocampal activation observed in the NSSI group was associated with increased emotion dysregulation. Despite its potential importance in understanding value-based decision-making in self-injurious thoughts and behaviors (Bettis et al., 2022), there has been a notable lack of investigation into the neural mechanisms of reward valuation in individuals with NSSI. This study provides the first evidence that individuals with NSSI exhibit significantly reduced neural responses when a positive outcome of a decision is not clearly guaranteed. This suggests that reduced valuation-related

Table 2. Brain regions of significant differences in fMRI task

Anatomical region		MNI coordinates			k	Peak Z
		x	y	z		
<i>Main effect of group</i> ^a						
Frontal						
Superior frontal gyrus	R	32	−2	68	100	4.12
Precentral gyrus	R	44	−14	64	84	3.78
Orbitofrontal cortex	L	2	50	−12	62	3.32
Occipital						
Occipital lobe	L	−4	−70	−6	266	4.92
	R	14	−74	−10	141	4.34
Temporal						
Fusiform gyrus	L	−24	−72	−14	79	3.81
<i>Main effect of condition</i> ^b						
Frontal						
Orbitofrontal cortex	L	6	36	2	777	6.29
Superior frontal gyrus	R	4	50	34	78	6.14
Parietal						
Precuneus	L	−6	−60	22	322	6.60
Inferior parietal gyrus	R	46	−38	46	101	6.14
Supramarginal gyrus	L	−62	−42	36	43	5.66
Occipital						
Occipital lobe	L	−10	−98	4	52	5.61
<i>Interaction effect of group-by-condition</i> ^a						
Cingulum						
Middle cingulate cortex	R	14	−42	36	149	4.08
Subcortical						
Hippocampus	L	−22	−30	−4	43	3.52

Notes. L/R, left/right hemisphere; MNI, Montreal Neurological Institute; k, cluster size.

^auncorrected $p < 0.005$, $k > 40$.

^bFWE-corrected $p < 0.05$, $k > 40$.

brain activation under uncertainty is related to inefficiencies in emotional processing in individuals with NSSI.

Regarding behavioral measures, there were no significant group differences in attitudes toward risk or ambiguity. This is consistent with previous studies using the Iowa Gambling Task, which failed to detect any differences in risky value-based decision-making between individuals who self-injured and controls under uncertainty (Janis & Nock, 2009; McCloskey, Look, Chen, Pajoumand, & Berman, 2012; Oldershaw et al., 2009; Schatten, Andover, & Army, 2015). Intriguingly, however, the level of ambiguity aversion in the NSSI group exhibited a compelling positive association with emotion reactivity and NSSI severity, as measured by NSSI versatility. No such correlations were observed for risk aversion in individuals with NSSI. These results suggest that heightened aversion to ambiguity may influence the severity of NSSI and the sensitivity, intensity, and persistence of emotions experienced by individuals with NSSI. In addition, given that reward learning under uncertainty has been linked to NSSI severity, as exemplified by NSSI recency (Oldershaw et al., 2009), further studies employing

value-based decision-making paradigms are necessary to understand the intricate psychopathology of NSSI.

At the neural level, we found significant group differences in the MCC and hippocampus during value-based decision-making under ambiguity compared to risk. Decision-making under uncertainty involves an interplay between emotion and cognition (Lerner, Li, Valdesolo, & Kassam, 2015; Schwarz, 2000). Furthermore, individuals with NSSI, relative to controls, have heightened emotional distress in uncertain circumstances (Ghaderi, Ahi, Vaziri, Mansouri, & Shahabizadeh, 2020). The MCC is known for its involvement in response selection (Vogt, 2005) and for its ability to mitigate conflicts arising from uncertainty (Grupe & Nitschke, 2013). In particular, the MCC plays a pivotal role in alleviating negative emotions associated with uncertainty through its robust connectivity with the amygdala and regions recruited during reward valuation under ambiguity, such as the prefrontal cortex and the anterior insula (Cauda et al., 2011; Moisset et al., 2010; Shackman et al., 2011). Thus, the diminished recruitment of MCC activation observed in

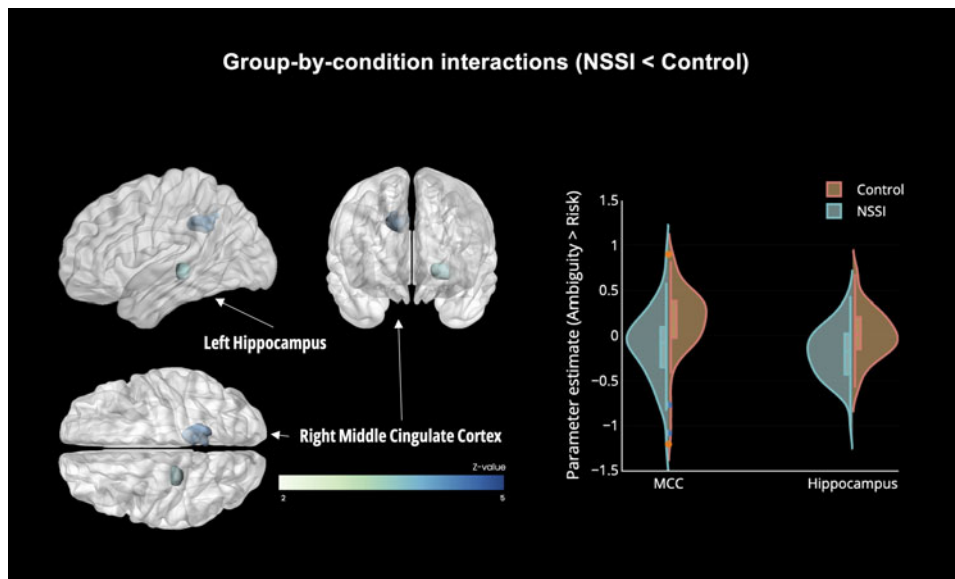


Figure 2. Significant group-by-condition interactions observed in the whole-brain ($p < 0.005$). Activation in the right middle cingulate cortex (MCC) and left hippocampus was decreased in the NSSI group compared to the control group during reward valuation under the condition of ambiguity compared to that of risk.

individuals with NSSI during reward valuation under ambiguity may indicate the potential neural mechanisms underlying the attenuated ability to regulate negative emotions when faced with ambiguous uncertainty. This finding contributes to our understanding of the neural basis of emotion dysregulation in NSSI, which is considered a core feature of this condition (McKenzie & Gross, 2014; Taylor et al., 2018).

The study found that individuals with NSSI showed reduced hippocampal activation during reward valuation under ambiguity and that this hippocampal hypoactivation is associated with emotion dysregulation in NSSI. The hippocampus incorporates future expectancies into current decision-making (Abela & Chudasama,

2013; Squire & Zola, 1996) by computing uncertainty signals (Eichenbaum, Dudchenko, Wood, Shapiro, & Tanila, 1999; Harrison, Duggins, & Friston, 2006) and encoding them into cognitive maps (Adcock, Thangavel, Whitfield-Gabrieli, Knutson, & Gabrieli, 2006; Soltani & Izquierdo, 2019). Recent data from the resting-state and gambling tasks of the Human Connectome Project (HCP) (Grill, Nyberg, & Rieckmann, 2021) also highlight hippocampus and ventral striatum recruitment in association with reward valuation, forming an intrinsic network. Thus, our finding of reduced hippocampal activation under ambiguity suggests that the neural vulnerability of individuals with NSSI in evaluating forthcoming reward outcomes and probabilities may contribute to emotion dysregulation.

In addition, our findings provide neural support for previous studies (In, Hur, Kim, & Lee, 2021; Wolff et al., 2019) demonstrating the effectiveness of Cognitive Behavioral Therapy (CBT) techniques in reducing cognitive distortions such as catastrophizing or overgeneralizing about the future in individuals with NSSI, thereby facilitating the rational appraisal of ambiguous situations. In the framework of CBT, the discussion of cognitive distortions emphasizes the individuals' tendency to interpret ambiguous events negatively (Leddy, Anderson, & Schulkin, 2013). For example, psychoeducation on cognitive distortions has been shown to effectively mitigate NSSI behaviors (Andover, Schatten, Morris, & Miller, 2015; Weismore & Esposito-Smythers, 2010). Additionally, cognitive reappraisal, which is achieved through repeated rehearsals to assess the possibility of catastrophic outcomes, leads to adaptive reward valuation. Notably, cognitive reappraisal is associated with the increased activation of a regulatory network involving the prefrontal and cingulate regions (Staudinger, Erk, Abler, & Walter, 2009). After the completing the CBT program, individuals with major depressive disorder showed enhanced functional connectivity between the dorsolateral prefrontal cortex and hippocampus, indicating improved cognitive control and affective processing (Wu et al., 2022). Collectively, incorporating the CBT strategies may enable individuals with NSSI to better evaluate future

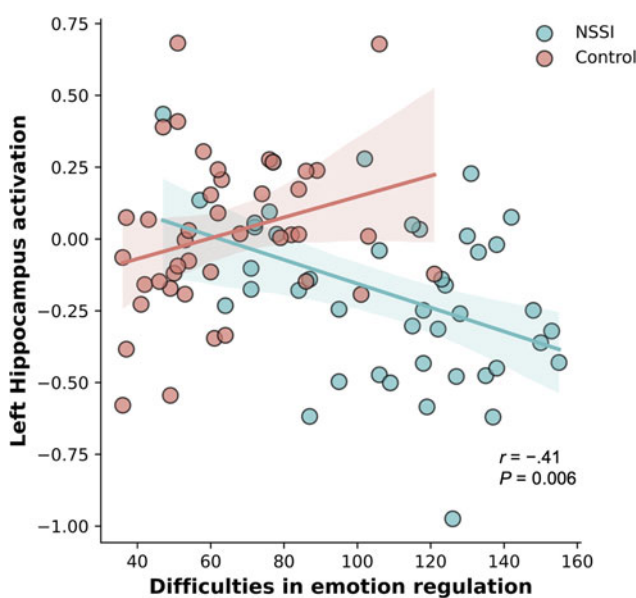


Figure 3. Scatterplots showing correlations between hippocampal activation and scores on the difficulties in emotion regulation scale. No significant correlation was found in the control group.

outcomes and possibilities through the enhanced neural processing efficiency.

Several limitations of this study should be considered when interpreting the results. First, the experimental condition consisted only of choices for gains, not losses. Consistent with previous research (Fujino et al., 2016; Levy et al., 2010), we accounted for cognitive fatigue in participants and designed the duration of the paradigm. To elaborate on the findings, it is necessary to examine the choice behavior of losses in future research efforts. Second, most participants in this study were highly educated individuals with an average range of cognitive functioning, which limits the generalizability of the sample. Similarly, to examine the physiological mechanisms of NSSI without considering the possible effects of medication or other interventions, we recruited only individuals who had not used psychotropic medication or received psychotherapy in the past month. Therefore, replicating our findings using a more diverse sample is imperative. Finally, these findings should be interpreted with caution as the comorbidity of individuals with NSSI were not controlled for. Given the transdiagnostic nature of NSSI, participants with comorbid psychiatric disorders were not excluded from the NSSI group. However, future studies should replicate our findings using larger samples that include clinical controls comprising individuals without NSSI but with a psychiatric diagnosis.

Despite these limitations, this study has important strengths. Previous studies on reward learning (Allen, Fox, Schatten, & Hooley, 2019; Janis & Nock, 2009; Schatten et al., 2015) and reward valuation (Janis & Nock, 2009) failed to reveal group differences between NSSI and controls at the behavioral level. However, insignificant differences at the behavioral level do not necessarily imply parallel results at the neural level, especially for individuals with clinical symptoms (Schweizer et al., 2019). Furthermore, as highlighted in a recent review, the majority of biological studies on NSSI lacked adequate sample sizes to rule out the possibility of type II errors (Kaess et al., 2021). The results of the present neuroimaging study, which included only unmedicated participants and had a robust sample size, demonstrated subtle alterations in the processing of reward valuation in NSSI, with significant implications for future research.

Conclusion

Understanding the underlying mechanisms of psychopathology is a prerequisite for developing evidence-based treatments, but the limited depth of our knowledge about NSSI poses a hurdle to devise effective interventions for individuals with NSSI. This study provides the first evidence of reduced activation in the MCC and hippocampus during value-based decisions in individuals with NSSI under ambiguity. Furthermore, this neural hypoactivation was found to be significantly associated with emotion dysregulation in NSSI. Our findings underscore the need for further efforts to support individuals with NSSI in pursuing rewarding experiences even amidst ambiguous uncertainty.

Funding statement. This research was supported by the National Research Foundation (NRF) funded by the Korean government (MSIT) (No. NRF-2022R1A2C2011467).

Competing interests. The author(s) declare none.

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