Prevention of depression in first-year university students with high harm avoidance
Evaluation of the effects of group cognitive behavioral therapy at 1-year follow-up

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Abstract
High harm avoidance (HA) scores on the temperament and character inventory appear to be a risk factor for depressive disorders and suicide. Since 2012, we have conducted group cognitive behavioral therapy (G-CBT) interventions for students at Nagasaki University with high HA and without depressive disorders, with the aim of preventing depression. Here, we report on the effects of the G-CBT at 1-year follow-up for the 2012 to 2015 period.

Forty-two participants with high HA were included in the final analysis. Outcomes were measured with the Beck Depression Inventory II, Manifest Anxiety Scale, 28-item General Health Questionnaire, and Brief Core Schema Scales at baseline, and at 6-month, and 1-year follow-ups.

Repeated-measures analyses of variance revealed a significant decrease in mean depressive symptom scores at the 6-month follow-up point; this decrease was maintained at 1 year. Improvements in cognitive schemas were also seen at 6 months and 1 year.

We observed improvements in cognitive schemas associated with depression as a result of the G-CBT intervention, with effects maintained at 1 year post-intervention. This intervention may be effective in positively modifying the cognitions of students with HA and preventing future depression.

Abbreviations: BCSS = Brief Core Schema Scales, BDI-II = Beck Depression Inventory II, CBT = cognitive behavioral therapy, G-CBT = group cognitive behavioral therapy, GHQ-28 = 28-item General Health Questionnaire, HA = harm avoidance, M.I.N.I. = Mini International Neuropsychiatric Interview, MAS = Manifest Anxiety Scale, RCTs = randomized controlled trials, TCI = temperament and character inventory.

Keywords: depression, group cognitive behavioral therapy, harm avoidance, high-risk approach, temperament and character inventory

1. Introduction
Psychiatric disorders can lead to prolonged absence or dropout among college students.[1] One such disorder is depression: major depressive disorder and depressive symptoms have clear effects on academic performance.[2] Individuals aged 15 to 21 years, especially university students, are at higher risk of a first episode of mental illness, with around 12% to 18% reporting a diagnosable mental disorder.[3,4] Although it is believed that there is a larger proportion of students with mild depression than with moderate or severe depression, mild depression is still considered a prodrome for major depressive disorder.[5]
Furthermore, experiencing depressive symptoms leads not only to psychological distress, but may also lead to learning difficulties, interpersonal relationship problems, various dependency problems, and many other issues (e.g., increased medical expenses).[6,7] Additionally, major depressive disorder and depressive symptoms are risk factors for suicide among university students.[8,9] Thus, depression prevention interventions targeting college students can be considered very important.

Research using the temperament and character inventory (TCI),[10,11] based on Cloninger personality theory, has revealed temperament and character factors relevant to depression and suicide.[12] The TCI comprises 4 temperament dimensions: novelty seeking, harm avoidance, reward dependence, and persistence. It also consists of 3 character dimensions: self-directedness, cooperativeness, and self-transcendence. Cloninger theory posits that personality is comprised of “temperament,” which has a hereditary physiological basis, and “character,” which relates to one’s self-concept and matures through insight and learning. Temperament
relates to our heritable tendency towards self-insight in response to certain behaviors, which in turn promotes character development. Furthermore, character is transformed according to a series of flows, which in turn can lead to changes in temperament. In sum, Cloninger considered personality to be the result of mutual interaction between temperament and character.\(^{[13]}\)

High scores on the temperament dimension of harm avoidance (HA) have been shown to predict major depressive disorder.\(^{[12,14]}\) HA relates to traits such as pessimism, worry, fear of uncertainty, shyness towards strangers, and tiring easily.\(^{[13]}\) In particular, when compared with healthy individuals, persons with major depressive disorder or bipolar disorder, and who have made suicide attempts, have higher HA.\(^{[15–17]}\) In Japan, high HA among college students has been reported as a risk factor for suicide.\(^{[18,19]}\) Patients with depression and high HA also tend to have a longer disease duration and greater suicide risk compared with low HA patients with depression. Moreover, HA levels remain high even after pharmacotherapy.\(^{[20–22]}\) Thus, high HA may be an important factor in identifying high-risk individuals for interventions targeting the prevention of depression and suicide.

According to guidelines on the treatment of depression, evidence-based psychotherapies, especially cognitive behavioral therapy (CBT), are treatment alternatives to antidepressants for evidence-based psychotherapies, especially cognitive Behavioral therapy (CBT).\(^{[23]}\) In some RCTs, group CBT (G-CBT) has also been studied with university students.\(^{[28,29]}\) Seligman et al.\(^{[28]}\) found that after G-CBT, students reported reduced mild depressive symptoms after 3 months, while Vázquez et al.\(^{[29]}\) found that both relaxation and G-CBT groups showed reductions in depressive and anxiety symptoms after 6 months. However, the G-CBT interventions in both of these RCTs targeted students with subthreshold depression, who represent a high-risk group due to the fact that they already have symptoms of depression. From the perspective of depression prevention, targeting university students without depressive symptoms may be more appropriate. Furthermore, no studies have yet investigated the effects of G-CBT at 1 year post-intervention in terms of changes in dysfunctional cognitions associated with depressive symptoms, despite such a study being necessary for the assessment of depression prevention.

In this context, we examined the effects of a G-CBT intervention on depression, at 1 year post-intervention, in university students without depressive symptoms.\(^{[27]}\) In some RCTs, group CBT (G-CBT) has also been studied with university students.\(^{[28,29]}\) Seligman et al.\(^{[28]}\) found that after G-CBT, students reported reduced mild depressive symptoms after 3 months, while Vázquez et al.\(^{[29]}\) found that both relaxation and G-CBT groups showed reductions in depressive and anxiety symptoms after 6 months. However, the G-CBT interventions in both of these RCTs targeted students with subthreshold depression, who represent a high-risk group due to the fact that they already have symptoms of depression. From the perspective of depression prevention, targeting university students without depressive symptoms may be more appropriate. Furthermore, no studies have yet investigated the effects of G-CBT at 1 year post-intervention in terms of changes in dysfunctional cognitions associated with depressive symptoms, despite such a study being necessary for the assessment of depression prevention.

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manual for therapists published by the Japanese Association for Cognitive Therapy (http://jact.umin.jp/pdf/cognitive_medical.pdf). The first session entailed education on the CBT theory of the relationship between negative automatic thoughts and psychological symptoms, as well as progressive muscle relaxation training. In the second to fourth sessions, participants were trained in cognitive restructuring using a 7-column technique aimed at changing their relationship to negative automatic thoughts. In the fifth session, participants were taught attribution theory, with a focus on how causal attribution leads to depressive symptoms and helplessness, and were then trained in causal therapy. In the final session, participants engaged in assertiveness training to improve their social skills.

The G-CBT program was conducted once a week over a 6-week period. Groups comprised 4 to 8 participants. Sessions generally lasted 60 minutes, except for the first and final sessions, which were each 90 minutes. Each G-CBT session was run by 2 trained university counselors.

3.2. Outcome measures
Outcome measures were administered at baseline (T0), 6-month follow-up (T1), and 1-year follow-up (T2). The primary and secondary outcomes are described below.

3.3. Primary outcome
3.3.1. Beck Depression Inventory II. The Beck Depression Inventory II (BDI-II) is a self-administered questionnaire comprising 21 items that assess depression severity. Each item is rated on a 4-point scale, and the range of total scores is 0 to 63. Cronbach \( \alpha \) for the Japanese version has been reported to be 0.87.[32]

3.4. Secondary outcomes
3.4.1. Manifest Anxiety Scale. The Manifest Anxiety Scale (MAS) is a self-administered questionnaire to assess anxiety symptoms; the original version comprises 50 items derived from the Minnesota Multiphasic Personality Inventory.[33,34] The Japanese version, in contrast, comprises 65 items, including the original 50 items and 15 items from the L scale, a validity scale of the Minnesota Multiphasic Personality Inventory.[35] For the Japanese version the Cronbach \( \alpha \) was 0.92.

3.4.2. Twenty-eight item General Health Questionnaire. The 28-item General Health Questionnaire (GHQ-28) is set of self-administered questionnaires that assess current physical and psychosocial problems.[36,37] The GHQ-28 comprises 4 subscales: somatic symptoms, anxiety and insomnia, social dysfunction, and depressive symptoms. The Cronbach \( \alpha \) for the Japanese version of the GHQ-28 total score in the present study was 0.77.

3.4.3. Brief Core Schema Scales. The Brief Core Schema Scales (BCSS) is a set of self-administered questionnaires measuring positive and negative schemas about the self and others.[38] The BCSS contains 24 items in total, and comprises 4 subscales: positive self-schemas, negative self-schemas, positive other-schemas, and negative other-schemas. The scoring system for the Japanese version is the same as the original. The Cronbach \( \alpha \) for the Japanese version was 0.92.[39] The BCSS was used to check for cognitive changes due to the G-CBT intervention. Participants completed the BCSS at baseline and at T1 and T2 follow-up points, but completion at T1 and T2 was voluntary.

3.5. Statistical analyses
All analyses were performed with SPSS 20.0 (SPSS, Inc., Chicago, IL). To determine the effect of the intervention, we conducted a repeated measures analysis of variance (ANOVA) with intervention time (T0, T1, and T2) for all outcome variables. Multiple comparisons between treatment periods were conducted using the Sidak post hoc test. We also calculated effect sizes of \( r^2 \) and Cohen \( d \). The effect sizes of \( r^2 \) indicate simple ANOVA main effect, where values around 0.01, 0.06, and 0.14 are considered small, medium, and large, respectively.[40] The Cohen \( d \) effect size values of 0.20, 0.50, and 0.80 are generally considered small, medium, and large, respectively.[41] Furthermore, we conducted a Pearson correlation analysis with the T0 and T2 scores of the Beck Depression Inventory (BDI), Manifest Anxiety Scale (MAS), 28-item General Health Questionnaire (GHQ-28), and Brief Core Schema Scales (BCSS) variables to examine their effects on BDI-II. Finally, we conducted a propensity score matching analysis to exclude selection bias for students with high HA that participated in the G-CBT intervention and those who did not receive treatment. The covariates were age, sex, 4 dimensions of temperament, and 3 dimensions of character from the TCI-R140J. In the present study, statistical significance was set at \( P < .05 \).

3.5.1. Ethics. This study was carried out in accordance with the Declaration of Helsinki. Additionally, the protocol complied with the Ethical Guidelines for Epidemiological Research and Guidelines for Clinical Research developed by the Ministry of Health, Labor, and Welfare by acquiring informed consent from all participants and protecting participants’ personal information. This study was approved by the ethics committee of the Nagasaki University Graduate School of Biomedical Sciences (approval number: 10033193).

4. Results
First, a total of 17 participants were excluded after baseline screening: 6 participants (6.9%) were aged over 22 years, and 11 participants (12.8%) provided incomplete baseline questionnaires. Second, a total of 27 participants were excluded after the G-CBT intervention: 8 participants (9.3%) were absent from more than half of the G-CBT sessions, and 19 participants withdrew (22.0%). Consequently, we analyzed the data of 42 participants (21 men, 21 women; mean age 18.97 ± 0.81 years) with completed questionnaires at T2 (Fig. 1). There were no statistically significant differences in sex ratio or ages of participants (\( x^2 (3) = 2.905, P = .407 \)).

Table 1 lists demographic data for study participants at T0. There were significant differences between men and women participants in novelty seeking (\( P = .002 \)), self-directedness (\( P = .003 \)), and self-transcendence (\( P = .015 \)). BDI, MAS, GHQ-28, and BCSS scores did not differ significantly between men and women participants.

The results for the primary outcome are shown in Table 2. BDI-II scores showed a simple main effect (\( P = .015 \)). Multiple comparison analysis showed significantly reduced scores at T1 compared with T0 (\( P = .025 \)), while there was no difference between T0 and T2 (\( P = .086 \)). Furthermore, BDI-II scores remained stable from T1 to T2 (\( P = .949 \)).

Manifest anxiety showed a marginally significant influence (\( P = .070 \)), but multiple comparison analysis showed no significant differences for T0 to T1 (\( P = .128 \)), T0 to T2 (\( P = .150 \)), and T1 to T2 (\( P = .985 \)) (Table 2).
Age, y 18.97 ± 0.81 (18.72–19.22) 19.00 ± 0.94 (18.56–19.43) 18.95 ± 0.66 (18.64–19.25) 0.18 .051 .12

Psychological symptoms and cognition after group cognitive behavior therapy treatment at 6 months and 1 year follow-up.

Variables presented as mean ± standard deviation and 95% confidence interval. Data were analyzed by Student t test. Men versus women.

Table 2

Psychological symptoms and cognition after group cognitive behavior therapy treatment at 6 months and 1 year follow-up.

The effect of G-CBT on the GHQ-28 is shown in Table 2. First, for GHQ-28 total score a simple main effect was observed (P = .010). Multiple comparison analysis showed significantly reduced GHQ-28 scores at T1 compared with T0 (P = .002), while there was no significant difference between T0 and T2 (P = .231). However, GHQ-28 total score increased significantly from T1 to T2 (P < .001). Second, the somatic symptoms subscale showed a marginally significant simple main effect (P = .063), but multiple comparison analysis was non-significant for all time periods. Third, the anxiety and insomnia subscale showed a simple main effect (P = .010). Multiple comparison analysis showed significantly reduced scores at T1 compared with T0 (P = .005), but no significant differences at T0 to T2 (P = .739) and T1 to T2 (P = .061). Fourth, the social dysfunction subscale...

| Variables | M (SD) | (95% CI) | M (SD) | (95% CI) | M (SD) | (95% CI) | F value | P value | Effect size |
|-----------|--------|----------|--------|----------|--------|----------|---------|---------|------------|
| T0        | T1     | T2       |        |          |        |          |         |         | (Cohen d)  |
| BDI-II    | 12.57 ±7.4 (10.15–14.98) | 9.11 ±10.36 (5.88–12.35) | 9.71 ±10.31 (6.50–12.92) | 4.39 .015 .09 .38 .01 .31 .06 .06 |
| GHQ-28 total score | 7.50 ±5.9 (5.75–9.24) | 5.17 ±5.01* (3.44–6.88) | 7.14 ±7.39* (4.83–9.44) | 4.89 .010 .10 .42 .06 .06 .30 .03 |
| Social functioning | 1.50 ±1.71 (0.96–2.03) | 1.00 ±1.54 (0.51–1.48) | 1.36 ±1.92 (0.75–1.95) | 2.17 .120 .05 .31 .08 .08 .21 .09 |
| Depressive symptoms | 1.26 ±2.10 (0.60–1.91) | 1.02 ±1.98 (0.40–1.64) | 1.43 ±2.38 (0.68–2.17) | 1.41 .248 .03 .12 .08 .08 .19 .19 |
| BSCS | 3.31 ±3.55 (2.20–4.41) | 5.86 ±5.44* (4.16–7.55) | 5.64 ±5.96* (3.96–7.35) | 9.10 .001 .18 .56 .51 .04 |
| Negative self-image | 9.04 ±5.41 (7.36–10.73) | 6.25 ±6.12* (4.69–8.59) | 7.48 ±6.34 (5.50–9.45) | 6.55 .002 .13 .41 .27 .13 |
| Positive other image | 5.87 ±4.35 (7.21–9.92) | 10.10 ±5.22 (8.46–11.72) | 10.26 ±5.12 (8.66–11.85) | 4.16 .019 .09 .32 .36 .03 |
| Negative other image | 2.21 ±4.87 (0.69–3.73) | 1.76 ±3.38 (0.70–2.81) | 2.49 ±4.96 (1.14–4.23) | 0.79 .456 .01 .11 .01 .02 .22 |

Variables are presented as mean ± standard deviation and 95% confidence interval. Data were analyzed by repeated ANCOVA followed by Bonferroni post-hoc test. Baseline versus 6 months follow-up and 1 year follow-up. Six months follow-up versus 1 year follow-up.

BDI-II = Beck Depression Inventory II; BSCS = Beck–Ruminative inventory; CBI = Cooperativeness; GHQ-28 = 28-item General Health Questionnaire; HA = Harm avoidance; MAS = Manifest Anxiety Scale; NS = novelty seeking; PD = Persistence; RD = Reward dependence; SD = Self-directedness; ST = Self-transcendence; T1 = baseline; T2 = 6 months follow-up; T3 = 1 year follow-up.

* P < .05.
** P < .01.
*** P < .001.
showed no simple main effect (P = .120). Finally, the depressive symptoms subscale also showed no simple main effects (P = .246).

The effect of G-CBT on core schemas is shown in Table 2. First, a simple main effect for positive self-image was observed (P < .001). Multiple comparison analysis showed significantly higher scores at T1 (P = .001) and T2 (P = .012) compared with T0, with no difference between T1 and T2 (P = .971). Second, a simple main effect was shown for negative other image (P = .002). Multiple comparison analysis showed significantly lower scores at T1 compared with T0 (P = .009), but no differences from T0 to T2 (P = .811), and T1 to T2 (P = .378). Third, a simple main effect was shown for positive other image (P = .019), but multiple comparison analysis revealed no significant differences for T0 to T1 (P = .065), T0 to T2 (P = .072), and T1 to T2 (P = .988). Finally, no simple main effect was shown for negative other image (P = .456).

We verified the treatment effect of G-CBT on BDI-II. We conducted correlation analyses with the T0 and T2 scores of the BDI-II, MAS, GHQ-28, and BCSS (Table 3). BDI-II scores were positively correlated with the negative self-image (r = 0.47, P = .002) subscale of the BCSS. Furthermore, BDI-II scores were negatively correlated with the positive self (r = -0.32, P = .042) and other image (r = -0.42, P = .005) subscales of the BCSS.

The 42 participants who participated in the G-CBT intervention were compared with 1065 participants who had high HA but did not participate in G-CBT. Table 4 presents the matched data of the propensity score analysis results. All scores were non-significant.

### 5. Discussion

Our results indicated that G-CBT for students with high HA, but without depressive symptoms, was effective in reducing BDI-II scores at 1 year post-intervention. BDI-II scores declined from T0 to T1, and maintained this improvement from T1 to T2. In terms of secondary outcomes, the MAS score was unchanged from T0 to T2. The GHQ-28 total score declined from T0 to T1, but this improvement was not maintained at T2. The GHQ-28 subscales did not change from T0 to T2, except for the anxiety and insomnia subscales. Scores for these subscales declined from T0 to T1, and maintained this improvement from T1 to T2. This may be explained as noted below.

### Table 3

| Correlation among changes of variables between baseline and 1 year follow-up. | BDI-II | MAS | Total score | SS | AI | SD | DS | BCSS |
|---|---|---|---|---|---|---|---|---|
| BDI-II | - | - | 0.56** | - | - | - | - | - |
| GHQ-28 Total score | 0.77** | 0.38* | - | - | - | - | - | - |
| SS | 0.52** | 0.34* | 0.73** | - | - | - | - | - |
| AI | 0.74 | 0.33** | 0.86 | 0.51** | - | - | - | - |
| SD | 0.53** | 0.30 | 0.78 | 0.42 | 0.59** | - | - | - |
| DS | 0.59** | 0.20 | 0.75 | 0.37 | 0.52** | 0.52** | - | - |
| PS | -0.32* | -0.82 | -0.32* | -0.08 | -0.17 | -0.34* | -0.48** | - |
| NS | 0.47** | 0.43** | -0.27 | 0.23 | 0.37** | 0.11 | -0.08 | -0.15 |
| PO | -0.42 | -0.19 | -0.39 | -0.20 | -0.36 | -0.39 | -0.28 | 0.39 | -0.34** |
| NO | -0.11 | 0.09 | -0.20 | 0.11 | -0.09 | -0.19 | -0.52 | 0.48 | 0.49 | -0.15 |

### Table 4

| Propensity score matching in the comparison of a non-participated to a HA participants. | Intervention group (N = 37) | Propensity score matching control group (N = 37) | Value | P value | Effect size (Cohen d) |
|---|---|---|---|---|---|
| Variables | M | SD | (95% CI) | M | SD | (95% CI) | | |
| Age, y | 18.81 | ±0.66 | (18.59–19.03) | 18.51 | ±0.73 | (18.26–18.75) | t=1.84 | .07 | .43 |
| Gender (N) male/female | 18/19 | 13/24 | 1.98 | .24 |
| TCI-R140J scores | | | | | | | |
| NS | 51.54 | ±5.57 | (49.68–53.39) | 50.51 | ±7.31 | (48.07–52.95) | t=0.68 | .50 | 0.16 |
| HA | 83.95 | ±5.30 | (82.17–85.71) | 85.03 | ±6.64 | (82.81–87.24) | t=0.77 | .44 | 0.18 |
| RD | 66.46 | ±10.32 | (63.01–69.90) | 67.16 | ±10.43 | (63.68–70.63) | t=0.29 | .77 | 0.07 |
| PS | 58.62 | ±9.55 | (55.43–61.80) | 57.78 | ±11.14 | (54.07–61.49) | t=0.35 | .73 | 0.08 |
| SD | 53.92 | ±11.73 | (50.00–57.82) | 53.05 | ±9.73 | (49.81–56.29) | t=0.35 | .73 | 0.08 |
| C | 71.14 | ±8.65 | (68.25–74.01) | 70.11 | ±10.17 | (66.71–73.49) | t=0.47 | .64 | 0.11 |
| ST | 35.54 | ±7.43 | (33.06–38.01) | 36.54 | ±8.12 | (33.83–39.24) | t=0.56 | .58 | 0.13 |

Variables are presented as mean ± standard deviation and 95% confidence interval. Data were analyzed with Student t test. Intervention group versus Propensity score matching control group.}

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First, the G-CBT intervention likely made it easier for participants to control their automatic thoughts, which coincides with Beck cognitive model of depression. Negative automatic thoughts can give rise to negative emotions and maladaptive behaviors, while cognitive reconstructing—a key aspect of G-CBT—can be used to reduce these negative automatic thoughts. Previous findings have indicated that reducing negative automatic thoughts results in an improvement in depressive symptoms. Second, our results may be due to the improvement in BCSS scores. Specifically, we observed increases in positive self-schema scores at T2 and a maintained reduction in negative self-schema scores at T1 to T2. According to Beck cognitive model of depression, maladaptive schemas are considered deeper-level constructs compared with automatic thoughts, whereby changes to schemas influence automatic thoughts, which in turn would lead to improvements in psychological symptoms (e.g., depression and anxiety). The fact that the G-CBT intervention influenced schemas even after 1 year may explain the sustained reduction in depressive symptoms.

Third, the results of the correlation analyses between the T0 and T2 treatment changes in the BDI-II, MAS, GHQ-28, and BCSS revealed that positive and negative self-schemas were associated with BDI-II scores. This suggests that self-schemas work to maintain depressive symptoms among university students. Furthermore, because the G-CBT intervention led to improvements in positive self-schemas, negative self-schemas, and depression scores, it is likely that it promoted depression prevention.

It is notable that none of our participants developed depressive disorders and were rather young, meaning that they experienced no degradation in cognitive functioning. This suggests that participants had relatively good cognitive flexibility, which may in turn suggest the possibility of cognitive plasticity. Thus, our results suggest that implementing G-CBT at an early stage may contribute to depression prevention in university students.

Finally, we must mention some of the limitations of this study. First, this was a single-arm study without a control group, and it did not use randomization. Therefore, it was not possible to adequately compare effects of improvements that may have been due to G-CBT. Second, we did not consider the effects of sex or age. Third, the intervention was conducted at a single facility at a regional university in Japan. Fourth, the intervention comprised a total of 6 sessions, which was fewer than the 8 sessions employed by Seligman et al. Finally, this study had a high attrition rate (39.1%). For that reason, we conducted propensity score matching analysis to examine differences in characteristics between the 42 participants who completed the study and 42 other students with high HA, and found no significant differences in sex, age, and TCI scores between the 2 groups. Additionally, submission of the BCSS was voluntary, and this may have increased attrition.

In future studies it will be important to recruit a control group for comparison purposes. Furthermore, because a university education typically spans 4 years, individuals will experience a variety of stressful experiences during that time. Therefore, it is necessary to investigate longer-term changes in the future.

6. Conclusion

To summarize, this G-CBT intervention led to decreases in depression scores compared with baseline, and these improvements were maintained at 1 year post-intervention. The G-CBT program also led to changes in schemas associated with depressive symptoms, which may have contributed to depression prevention.

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