



BRIEF REPORT

Cyclothymic Temperament is Associated with Poor Medication Adherence and Disordered Eating in Type 2 Diabetes Patients: A Case–Control Study

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ABSTRACT

Introduction: Poor medication adherence and disordered eating are major self-care problems

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in patients with type 2 diabetes that worsen glycemic control and increase the risk of developing severe diabetes complications. Affective temperament, which remains mostly unchanged throughout life, is speculated to predict poor treatment response and high comorbidity. The aim of this study was to explore the link between affective temperament and poor glycemic control due to insufficient self-care.

Methods: This single-center case–control study involved 77 outpatients divided into the ‘poor glycemic control’ group ($n = 52$) and the ‘better glycemic control’ group ($n = 25$) based on their mean glycated hemoglobin (HbA1c) levels over the past 12 months. All participants underwent one-on-one interviews during which they completed the following psychometric questionnaires: (1) the Mini-International Neuropsychiatric Interview 5.0.0; (2) the Temperament Evaluation of Memphis, Pisa, and San Diego Auto-questionnaire; (3) a researcher-designed single question for assessing subclinical stress-induced overeating; and (4) the Morisky Medication Adherence Scale. The difference between two continuous independent variables was determined using Student’s t test. Discrete variables were compared using the Chi-square (χ^2) or Fisher’s exact test. Multiple testing corrections were performed using the false discovery rate.

Results: Those outpatients in the poor glycemic control group exhibited significantly

more stress-induced overeating ($\chi^2 = 1.14$, q statistic = 0.040) and poor medication adherence ($t = 3.70$, $q = 0.034$) than those in the better glycemic control group. However, there were no significant differences between the two groups in terms of affective temperaments, clinical eating disorders, or diabetes-specific distress. Patients with stress-induced overeating ($t = -2.99$, $p = 0.004$) and poor medication adherence ($t = -4.34$, $p = 0.000$) exhibited significantly higher scores for cyclothymic temperament than their counterparts.

Conclusion: Cyclothymic temperament is significantly associated with disordered eating and/or poor medication adherence in patients with type 2 diabetes and is possibly linked to poor glycemic control.

Keywords: Affective temperament; Bipolar II disorders; Cyclothymic temperament; Depression; Disordered eating; Poor glycemic control; Poor medication adherence; Stress-induced overeating; TEMPS-A; Type 2 diabetes

Key Summary Points

Why carry out this study?

Poor medication adherence and disordered eating are major self-care problems in patients with type 2 diabetes (T2DM) because they worsen glycemic control, thereby increasing the risk of severe diabetes complications. On the contrary, affective temperament, which determines response to internal and external stress and remains mostly unchanged throughout life, can chronically influence self-care behaviors and glycemic control.

To date, there have been no published clinical studies aimed at comprehensively investigating the association between affective temperament, self-care problems, and poor glycemic control.

This study aimed to examine our hypothesis that affective temperament is a common cause of disordered eating and poor medication adherence and is thus placing these patients at risk of poor glycemic control.

What was learned from the study?

The 'poor glycemic' control group demonstrated significantly more stress-induced overeating ($\chi^2 = 1.14$, q statistic = 0.040) and poor medication adherence ($t = 3.70$, $q = 0.034$) than to those in the 'better control' group; however, there were no significant differences between the two groups in terms of affective temperaments, clinical eating disorders, or T2DM-specific distress.

Cyclothymic temperament, a subtype of affective temperament, may be responsible for disordered eating and poor medication adherence in patients with T2DM and is possibly linked with poor glycemic control.

INTRODUCTION

The management of type 2 diabetes mellitus (T2DM) requires blood glucose levels to be maintained within the optimal glycemic range to avoid complications. However, long-term optimal glycemic control is difficult to maintain [1], and more than 30% of the patients with diabetes do not attain their individual glycemic goals [2]. Effective self-management of diabetes is essential to achieve optimal glycemic control and requires behavioral changes and/or adaptations [3].

The most common problems with self-management in patients with T2DM include poor medication adherence [2] and disordered eating [4], both of which result in poor glycemic control. Previous studies suggest that disordered eating affects up to 50% of the patients with T2DM [4] and is associated with increased

retinopathy and neuropathy [5, 6] along with increased morbidity and mortality, high costs of outpatient care, and poor management of diabetes-associated complications [7].

Self-care behaviors and their subsequent medical outcomes in patients with T2DM are substantially influenced by complex individual, environmental, social, behavioral, and psychological factors [8]. While many studies have been conducted on the association between psychological factors and diabetes, including topics such as depression [9, 10], anxiety [11], chronic stress [12], anger [13], hostility [14], and diabetes-related distress [15], most have focused on the impact of these factors on diabetes onset, with only few exploring the psychological factors, such as temperament, which chronically influence self-care behaviors and glycemic control.

Temperament determines one's response to internal and external stimuli and remains mostly unchanged throughout life [16]. Therefore, problems with self-care behaviors attributed to temperament are difficult to change and can lead to long-term poor glycemic control. Affective temperament, conceptualized by Akiskal et al. [17] as characterized by depressive, hyperthymic, cyclothymic, irritable, and anxious types has gained the attention of researchers, and various studies have been conducted to associate these concepts with physical disease. One study reported that affective temperaments play a role in developing hypertension and arterial stiffening [18], whereas another study suggested that patients with T2DM and a depressive or anxious temperament exhibited poorer self-care behavior and metabolic control than patients without predominant affective temperaments [19].

To the best of our knowledge, no study has comprehensively analyzed the association of glycemic control, critical self-care behaviors, such as disordered eating and poor medication adherence, and affective temperaments. Therefore, the aim of this study was to clarify this association, employing structured interviews to differentiate clinically diagnosable affective disorders and eating disorders from subclinical statuses such as affective temperaments and disordered eating behaviors.

METHODS

Ethics

This study and its protocols were approved by the institutional review board of Chiba University School of Medicine (Reference No. 2175) and Kimitsu Chuo Hospital (Reference No. 272) in accordance to the Ethical Guidelines for Medical and Health Research Involving Human Subjects issued by the Ministry of Health, Labour and Welfare of Japan. The study was conducted in accordance with the Declaration of Helsinki 1964 and its later amendments; the Ethical Guidelines for Medical and Health Research Involving Human Subjects issued by the Ministry of Health, Labour and Welfare of Japan; the Clinical Trials Act; and other current legal regulations in Japan. Written informed consent was obtained from all participants after a providing them full explanation of this study, and all participants provided consent to participate. Authorization to use of MMAS-4 in this study was granted by Prof. DE Morisky, MMAS Research, LLC.

Study Design and Recruitment Criteria

This was a single-center case-control study. All patients with T2DM (aged 18–75 years) who had been attending the Department of Diabetes, Endocrinology, and Metabolism of Kimitsu Chuo Hospital for at least 3 years since September 2015 were screened for eligibility to participate in the study. The medical records of 905 patients with laboratory data from the 3 previous years and at least six glycated hemoglobin (HbA1c) measurements over the past 12 months were screened and relevant data extracted. Patients with a mean HbA1c $\geq 8.5\%$ over the past 12 months (12mAv-HbA1c) were included in the 'poor glycemic control' group (PG), and those with 12mAv-HbA1c levels $< 7.5\%$ were included in the 'better glycemic control' group (BG). Patients with 12mAv-HbA1c levels between 7.5 and 8.5% were not included in the study since our aim was to focus on patients in the PG, a patient group that diabetologists have the most difficulty in

helping achieve optimal glycemic control compared with patients with better glycemic control.

We estimated that the maximum number of one-on-one structured interviews we could conduct during the study period would be approximately 150; hence, we planned to recruit approximately 250 patients with T2DM to select the study participants. In the PG, we selected all 63 patients who suffered more than one diabetes complication as a predictive factor for long-term poor glycemic control, and among the remaining patients in the PG, we randomly selected 100 patients. Similarly, 100 patients of the BG were randomly selected. The purpose of the study was explained to all 263 patients. The exclusion criteria were: steroid therapy, dementia or schizophrenia, conditions that involve neurological manifestations (such

as thyroid dysfunction, adrenal dysfunction, and collagen disease), hospital transfer, mortality, or discontinuation of treatment during the study period. A flowchart of the sampling procedure is shown in Fig. 1.

Assessment of Clinical Characteristics

Age, sex, duration of diabetes, history of psychiatric medication, and use of psychotropic medicines (antidepressants, mood stabilizers, and antipsychotics), some of which have adverse metabolic effects and worsen glycemic control, were assessed using a standardized questionnaire. We verified the use of insulin and/or glucagon-like peptide-1 (GLP-1) receptor agonist injection therapy and body mass index (BMI; kg/m²) from medical charts.

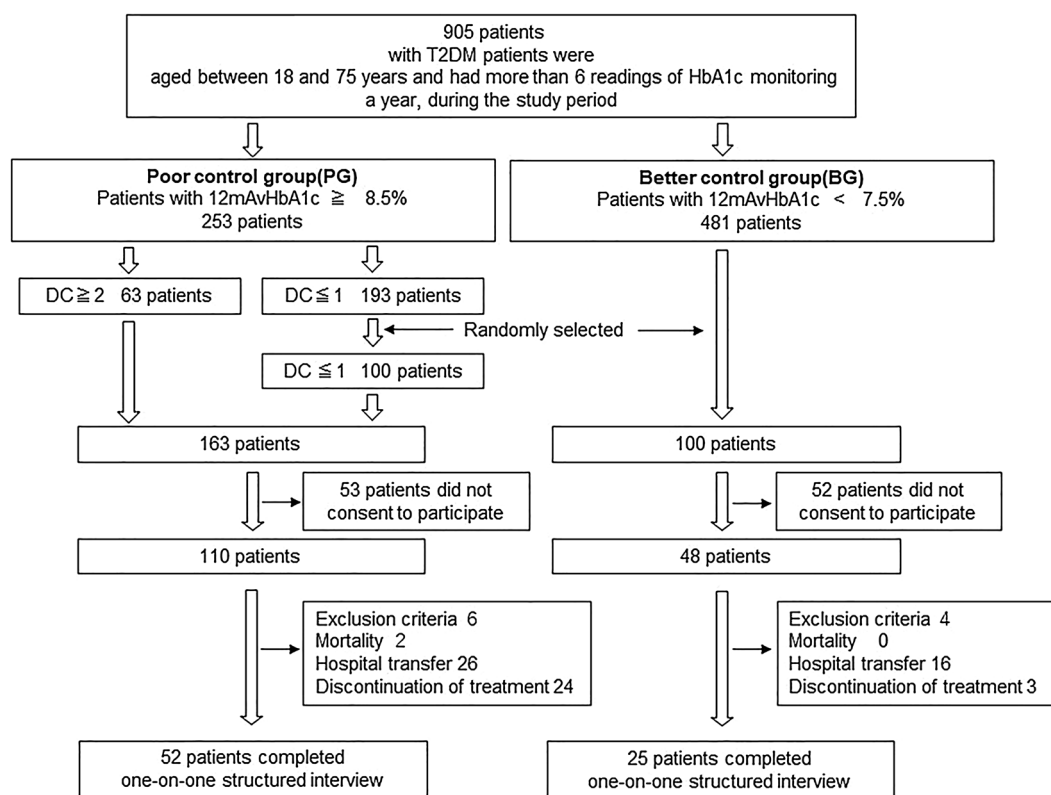


Fig. 1 Flowchart of patient sampling procedure. *DC* Diabetes complication, including diabetic nephropathy, diabetic retinopathy, and diabetic neuropathy, *BG* 'better glycemic control' group, *2mAv-HbA1c* mean HbA1c over

the past 12 months, *HbA1c* glycated hemoglobin, *PG* 'poor glycemic control' group, *T2DM* type 2 diabetes mellitus

Assessment of Psychological Conditions

Bipolar I disorder, bipolar II disorder, major depressive disorder, bulimia nervosa, and binge eating disorder were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM–5), Fifth Edition (DSM-5; American Psychiatric Association, Washington DC, USA) and Mini-International Neuropsychiatric Interview 5.0.0 scores. Affective temperaments were evaluated using the full version of the Temperament Evaluation of Memphis, Pisa, and San Diego Auto-questionnaire (TEMPS-A) [20], which is a true–false self-reporting questionnaire comprising 110 questions that evaluate affective temperaments, including depressive, cyclothymic, hyperthymic, irritable, and anxious temperaments. The reliability and validity of the Japanese version of TEMPS-A have been established [21]. Temperament scores were converted into categorical variables with a cutoff point corresponding to a z-score of 1, which is the minimum value that indicates excessive temperament. Regarding subclinical disordered eating, the researcher-designed question, “Have you experienced uncontrollable overeating as a reaction to a preceding stress-event or mood change?” was asked to confirm the presence or absence of stress-induced overeating [22] and/or mood instability. Medication adherence was evaluated using the Japanese translation of the 4-item Morisky Medication Adherence Scale (MMAS) [23–27].¹

Statistical Analysis

The difference between two continuous independent variables was determined using Student’s *t* test. Comparisons between two discrete variables were made using the chi-square test or Fisher’s exact test. To evaluate the effects of affective temperaments on self-care behaviors, the TEMPS-A scores of each temperament were

converted into z-scores before performing the Student’s *t* test, which was then used to compare the difference between the two stress-induced overeating groups and also between the two MMAS-4 groups. The two groups of each variable were defined as follows: stress-induced overeating was divided based on its existence (yes vs. no); MMAS-4 score was divided into two groups based on scores (better medication adherence [BA] = 0 or 1 vs. poor medication adherence [PA] = 2–4). The Japanese translation of the MMAS-4 had not yet been validated at the time of the survey; therefore, we used these cutoff values because approximately 80% of the participants in our study had a score of 0 or 1.

Multiple testing corrections were performed using the false discovery rate (Benjamini–Hochberg method), with appropriate *p* values determined using two-tailed tests and *q* values < 0.1 considered to indicate significance. We constructed a path model using structural equation modeling (SEM), which posited that long-term glycemic control was associated with self-care behaviors and affective temperaments. Statistical analyses were performed using SPSS version 19 (SPSS-IBM, Armonk, NY, USA) and R (package version 3.6.1; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Participants

In total, 263 patients with T2DM received an explanation on the purpose of the study, and 158 agreed to participate. Among these 158 patients, ten individuals who met the exclusion criteria were excluded from the interview, and 71 individuals (2 deaths, 42 hospital transfers, and 24 who discontinued treatment) dropped out from the study after initiating the survey. Ultimately, 52 patients in the PG group and 25 patients in the BG group completed the survey. The sampling procedures by group are shown in Fig. 1.

A comparison of the attributes and variables of participants in the PG and BG groups is presented in Table 1. There was no significant

¹ (Note: The MMAS-4 Scale, content, name, and trademarks are protected by US copyright and trademark laws. Permission for use of the scale and its coding is required. A license agreement is available from MMAR, LLC., Donald E. Morisky, ScD, ScM, MSPH, 294 Lindura Ct., USA; donald.morisky@moriskyscalel.com.)

Table 1 Demographic and medication variables according to mean glycated hemoglobin values over the past 12 months of < 7.5% (better glycemic control group) and \geq 8.5% (poor glycemic control group)

Variables	Better glycemic control group (12mAv-HbA1c < 7.5%), <i>n</i> = 25	Poor glycemic control (12mAv-HbA1c \geq 8.5%), <i>n</i> = 52	Statistics
Age, mean (SD)	60.9 (13.6)	58.0 (13.9)	$t = 0.9, p = 0.39$ $q = 0.737$
Female, %	52.0	40.0	$\chi^2 = 0.895, p = 0.81$ $q = 1.000$
Duration of diabetes, years, mean (SD)	14.5 (9.5)	17.1 (10.0)	$t = 1.1, p = 0.28$ $q = 0.595$
BMI, mean (SD)	27.3 (4.1)	27.2 (5.1)	$t = 0.1, p = 0.89$ $q = 1.000$
Use of injection therapy ^a , %	34.7	71.4	$\chi^2 = 9.49, p = 0.003$ $q = 0.034^*$
History of psychiatric medication, %	24.0	7.7	$\chi^2 = 2.12, p = 0.07$ $q = 0.300$
Use of antidepressants, %	0	0	–
Use of antipsychotics, %	0	0	–

12mAv-HbA1c Mean HbA1c over the past 12 months, BMI body mass index, FDR false discovery rate, q q statistic, SD standard deviation

* $q < 0.1$

^a Injection therapy includes insulin and glucagon-like peptide-1 analogs

difference between the two groups in terms of age, sex, duration of disease, and current BMI. The use of insulin and/or GLP-1 receptor agonist injection therapy was significantly higher in the PG group than in the BG group (34.7 vs. 71.4%, $q = 0.034$).

Glycemic Control and Self-care Behaviors

Regarding self-care behaviors, patients in the PG group exhibited significantly higher stress-induced overeating ($\chi^2 = 1.14, q = 0.040$) and poorer medication adherence ($t = 3.7, q = 0.034$) than those in the BG group. However, there was no significant difference between the groups in terms of clinical eating disorders.

Psychiatric/Psychological Factors in the PG and BG groups

There was no significant difference in both the history of psychiatric medication and the use of psychotropic medicines, such as antidepressants, mood stabilizers, and antipsychotics, between the two groups. No patient was diagnosed with bipolar I disorder according to Table 2 in either group. Although several psychological conditions were identified in both groups, there was no significant difference between the patients in the BG and PG groups in terms of prevalence of bipolar II disorder according to Table 2 (4.5 vs. 7.5%, $q = 1.000$), major depressive disorder (18.2 vs. 7.5%, $q = 1.000$), bulimia nervosa (0.0 vs. 5.4%,

$q = 0.819$), and binge eating disorder (0.0 vs. 10.5%, $q = 0.819$).

Affective Temperament in the PG and BG groups

In this study, there was no significant difference between the BG and PG groups regarding the following predominant affective temperaments: depressive (9.1 vs. 25.6%, $q = 0.408$), cyclothymic (13.6 vs. 15.3%, $q = 1.000$), hyperthymic (9.1 vs. 20.5%, $q = 0.595$), irritable (13.6 vs. 17.9%, $q = 0.935$), and anxious (27.3 vs. 15.3%, $q = 0.595$).

Association Between Self-care Behaviors and Affective Temperaments

The group with stress-induced overeating showed a higher cyclothymic temperament score than did the group without stress-induced overeating (z-score: 0.391 vs. -0.332 , $p = 0.004$); however, there were no differences in other temperaments between the groups (Fig. 2). In addition, patients categorized in the group with poor medication adherence had significantly higher scores for cyclothymic temperament (z-score: 1.133 vs. -0.227 , $p = 0.000$) than those categorized in the group with better medical adherence, while other temperaments did not differ between the groups (Fig. 3).

Association Between Injection Therapy and Self-care Behaviors

Poor self-care behaviors, such as disordered eating and poor medication adherence, are considered to be associated with diabetes injection therapy [28, 29]. However, in our study, there was no significant association between these behaviors and injection therapy, as shown in Electronic Supplementary Material Table S1.

Relationship between Affective Temperaments, Self-care Behaviors, and Glycemic Control

Path analysis using SEM was performed to evaluate the hypothetical pathway from cyclothymic temperament that was significantly associated with disordered eating and poor medication adherence in our analysis of glycemic control through self-care behaviors. The model shown in Fig. 4 accurately illustrates the data according to all goodness-of-fit measures: model $\chi^2 = 0.5444$, $df = 3$, $p = 0.909$, Akaike information criterion (AIC) = 14.544, and Bayesian information criterion (BIC) = -11.478 . The path coefficients of cyclothymic temperament toward stress-induced overeating (0.449, $p < 0.001$) and medication adherence (0.498, $p < 0.001$), as well as that of medication adherence toward 12mAv-HbA1c (0.408, $p < 0.001$), were highly significant. The path coefficient of stress-induced overeating toward 12mAv-HbA1c was not significant (0.228, $p = 0.056$) but showed a potential association.

DISCUSSION

In this study we tested the hypothesis that disordered eating and poor medication adherence, which are regarded as critical self-care behaviors that influence glycemic control, may be significantly affected by emotional factors. In particular, affective temperament could chronically affect these self-care behaviors, resulting in poor long-term glycemic control. The results suggest that in our patient population: (1) disordered eating and poor medication adherence were significantly associated with poor glycemic control; and (2) cyclothymic temperament—a type of affective temperament—was significantly associated with disordered eating and PA; in addition, (3) the SEM analysis indicated that there is a possible causal linkage between cyclothymic temperament and poor glycemic control modulated by disordered eating and poor medication adherence.

Individuals with cyclothymic temperaments begin to show clinical characteristics from their

Table 2 Psychological and self-care behavior variables according to 12mAv-HbA1c values < 7.5% (better glycemic control group) and \geq 8.5% (poor glycemic control group)

Variables	Better glycemic control group (12mAv-HbA1c < 7.5%), <i>n</i> = 25	Poor glycemic control group (12mAv-HbA1c \geq 8.5%), <i>n</i> = 52	Statistics
Bipolar I disorder, %	0.0	0.0	–
Bipolar II disorder, %	4.5	7.5	$\chi^2 = 0.20, p = 1.00$ $q = 1.000$
Major depressive disorder, %	18.2	7.5	$\chi^2 = 0.20, p = 1.00$ $q = 1.000$
Depressive temperament ^a , %	9.1	25.6	$\chi^2 = 2.40, p = 0.12$ $q = 0.408$
Cyclothymic temperament ^a , %	13.6	15.3	$\chi^2 = 0.93, p = 0.85$ $q = 1.000$
Hyperthymic temperament ^a , %	9.1	20.5	$\chi^2 = 1.34, p = 0.25$ $q = 0.595$
Irritable temperament ^a , %	13.6	17.9	$\chi^2 = 0.19, p = 0.66$ $q = 0.935$
Anxious temperament ^a , %	27.3	15.3	$\chi^2 = 1.26, p = 0.26$ $q = 0.595$
Bulimia nervosa, %	0.0	5.4	$\chi^2 = 1.18, p = 0.53$ $q = 0.819$
Binge eating disorder, %	0.0	10.5	$\chi^2 = 102.4, p = 0.53$ $q = 0.819$
Stress-induced overeating, yes, %	22.8	60.0	$\chi^2 = 1.14, p = 0.007$ $q = 0.040^*$
MMAS-4 score, mean (SD)	1.3 (1.2)	3.4 (3.1)	$t = 3.7, p = 0.004$ $q = 0.034^*$

MMAS-4 Morisky Medication Adherence Scale

* $q < 0.1$

^a Temperament Evaluation of Memphis, Pisa, and San Diego Auto-questionnaire (TEMPS-A)

teens into early adulthood. Such individuals experience both manic and depressive phases, such as lassitude and physical discomfort versus feeling good and having pessimistic thoughts versus a tendency for overoptimism accompanied by a lack of concern, all of which can

potentially lead to painful consequences. Generally, each phase lasts only a few days, contributing to a relatively unstable mood [17].

Several studies have demonstrated a positive association between cyclothymic temperament and eating disorders. Ramacciotti et al.

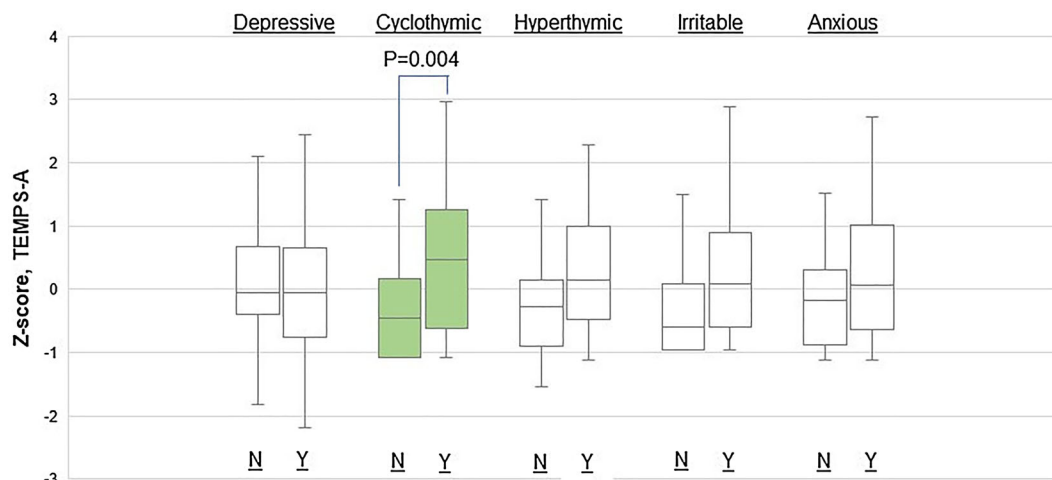


Fig. 2 Box plot of presence of stress-induced overeating. Stress-induced overeating can be seen to have a significant relationship with cyclothymic temperament (boxplot in green). Scores of the Temperament Evaluation of Memphis, Pisa, and San Diego Auto-questionnaire

(*TEMPS-A*) were converted into *z*-scores, and the Student’s *t* test was performed using the averages of *z*-scores for comparing groups according to the presence (yes [*Y*]) or absence (no [*N*]) of stress-induced overeating

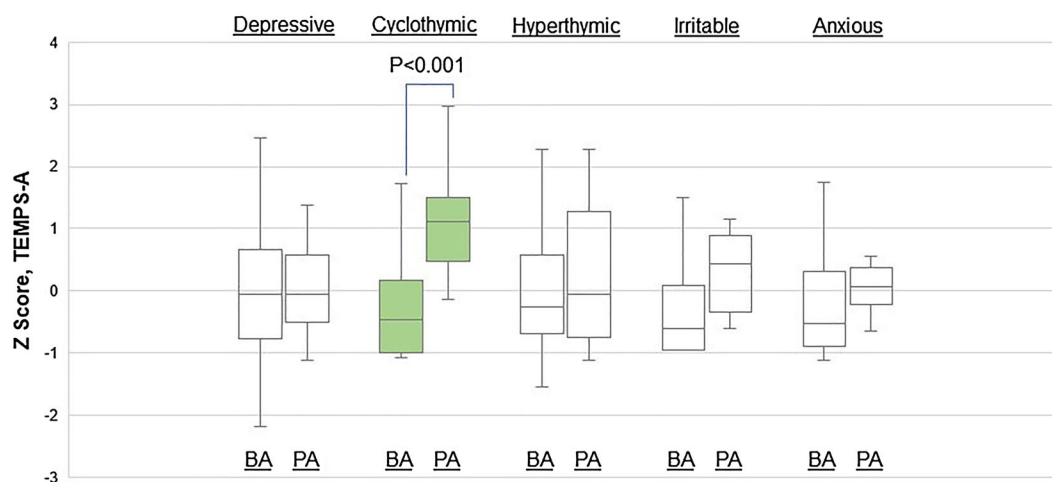


Fig. 3 Box plot of TEMPS-A scores between the better medication adherence (*BA*) group and the poor medication adherence (*PA*) group. Poor medical adherence can be seen to have a significant relationship with cyclothymic temperament (boxplot in green). TEMPS-A scores were

converted into *z*-scores, and the Student’s *t* test was performed using the averages of *z*-scores to compare better the *BA* group (score = 0 or 1) with the *PA* group (score = 2 to 4), categorized by the Morisky Medication Adherence Scale (MMAS-4) score

investigated the affective temperaments in a sample of patients with eating disorders and identified that only cyclothymic temperament was significantly higher in the binge eating subgroup [30]. D’Ambrosio et al. investigated

affective temperaments and clinical characteristics in patients with obsessive/compulsive disorders and found that patients with cyclothymic temperament showed significantly more repeating compulsions and higher

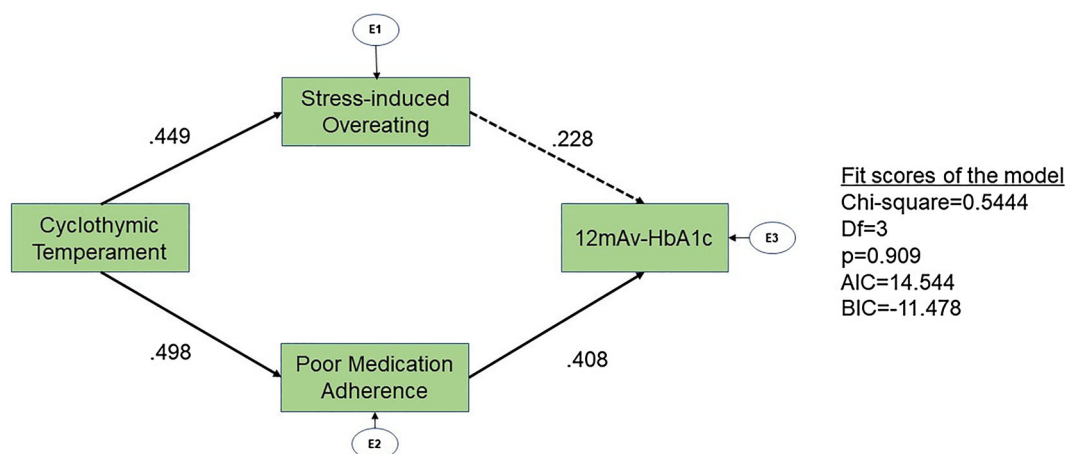


Fig. 4 Structure equation model with 12mAv-HbA1c, stress-induced overeating, MMAS-4 score, and cyclothymic temperament as per the TEMPS-A score. The arrows with solid lines represent significant pathways, and the arrow

with the broken line represents a non-significant pathway. The number beside the arrows indicates the standardized path coefficient (minimum -1 , maximum 1). *E1*, *E2*, *E3* Error variables

comorbidity rates with eating disorders than did other patient groups [31].

As a background of these associations, the following psychopathological process is assumed. People with cyclothymic temperament are impulsive and prone to addiction to control mood instability [32]. Psychological stress associated with mood instability may predispose patients to stress-induced overeating, with acceleration in the consumption of energy- and nutrient-dense processed foods that have high sugar and fat content [33] and considered to be addictive substances [34]. Specifically, instead of dealing with mood instability appropriately, these people tend to engage in “dysfunctional mood modulatory behaviors,” such as overeating, which may reduce awareness of mood status and neutralize the distress of mood change [35]. Continuous overeating of nutrient-dense processed foods may pose addictive and long-lasting disordered eating. Additionally, the constitutional disposition of overoptimism and risk-taking represented in cyclothymic temperament may influence the long-term course of refined food addiction [32, 34] and poor medication adherence. Although our study has not investigated the chronicity of disordered eating and poor medication adherence, symptomatic traits of cyclothymic temperaments, such as mood

instability, impulsivity, and overoptimism, may induce or prolong disordered eating and/or poor medication adherence and subsequently lead to poor glycemic control.

In contrast, it is also essential for clinicians to know that patients with cyclothymic temperament are possibly in the subclinical phase of bipolar disorder or may develop bipolar disorder in the future [17, 36–38]. In addition to cyclothymic temperament, we identified patients with undiagnosed bipolar II disorder in this study. Individuals with bipolar II disorder may show only depressive symptoms in the subclinical phase; however, indiscriminate use of antidepressants may increase agitation risk in these patients [39]. Therefore, this psychological state requires the attention of clinicians.

In contrast, however, we previously reported a case [40] in which never-diagnosed bipolar II disorder was identified in a patient with T2DM with a chronic eating disorder and poor glycemic control. Treatment with a mood-stabilizer resulted in a remarkable improvement in both the eating disorder and glycemic control.

In summary, identifying cyclothymic temperament in patients with T2DM will allow clinicians to address long-term disordered eating, poor medication adherence, and poor glycemic control. Furthermore, referral of patients with severe symptoms of cyclothymic

temperament to a mental health professional may increase their chances to improve self-care behaviors and glycemic control with appropriate medication in case the patient has a comorbid affective disorder.

To assess cyclothymic and other temperaments, TEMPS-A short-version [41], which comprises 39 items instead of the 110 items in the full version), may have better usability. Moreover, further development of more straightforward and usable questionnaires that could distinguish cyclothymic temperament in patients with T2DM is required. This may include a combination of TEMPS-A and questionnaires to assess disordered eating and poor medication adherence.

This study has several strengths. First, both poor medication adherence and disordered eating, which are two key risk factors for poor glycemic control that are commonly observed in clinical settings, were investigated. Second, we used a standardized structured interview to distinguish diagnosable affective/eating disorders, subthreshold affective conditions, and disordered eating. Third, we used the 12mAv-HbA1c, which reflects the status of the year-long self-care management.

This study also has several limitations. First, this was a single-center study with small sample size. We did not perform a power analysis at the beginning of the study because it was challenging to formulate the sample design owing to the lack of previous studies with similar objectives. Hence, we considered the current study to be a pilot study and conducted one-on-one structured interviews, which, in effect, limited the total sample size due to the time-consuming nature of this type of interview. Since our study's sample size was small, the results may not adequately reflect the difference in affective temperament between the PG and BG. Nevertheless, our findings may be used as a basis for larger studies. Second, the general population was not included. We also did not establish the validity and reliability of the researcher-made questionnaire. Future studies should be performed with larger samples covering the general population and more detailed and reliable indices of eating behaviors.

CONCLUSIONS

Cyclothymic temperament is significantly associated with disordered eating and poor medication adherence, which are major causes of poor glycemic control among patients with T2DM. Our findings can potentially convince clinicians of the necessity of increasing their awareness of the cyclothymic temperament and its relationship with T2DM and affective disorders. This awareness may contribute towards the patient achieving optimal glycemic control and receiving appropriate psychiatric treatment if necessary.

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Authors' Contributions. Tetsuya Yamamoto developed the concept of this research, and Tetsuya Yamamoto, Kenichi

Sakurai, Masahiro Watanabe, Ikki Sakuma, Nobuhisa Kanahara, Akihiro Shiina, Tadashi Hasegawa, Hiroyuki Watanabe, Masaomi Iyo, Ryoichi Ishibashi designed the study. Tetsuya Yamamoto researched the data. Masahiro Watanabe was in charge of the statistical analysis. Tetsuya Yamamoto, Kenichi Sakurai, Masahiro Watanabe, Ikki Sakuma, Nobuhisa Kanahara, Akihiro Shiina, Tadashi Hasegawa, Hiroyuki Watanabe, Masaomi Iyo, and Ryoichi Ishibashi wrote the manuscript.

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Compliance with Ethics Guidelines. This study and its protocols were approved by the institutional review board of Chiba University School of Medicine (Reference No. 2175) and Kimitsu Chuo Hospital (Reference No. 272) in accordance to the Ethical Guidelines for Medical and Health Research Involving Human Subjects issued by the Ministry of Health, Labour and Welfare of Japan. The study was conducted in accordance with the Declaration of Helsinki 1964 and its later amendments; the Ethical Guidelines for Medical and Health Research Involving Human Subjects issued by the Ministry of Health, Labour and Welfare of Japan; the Clinical Trials Act; and other current legal regulations in Japan. Written informed consent was obtained from all participants after a providing them full explanation of this study, and all participants provided consent to participate. Authorization to use of MMAS-4 in this

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Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available owing to the lack of approval for data sharing from the institutional review board of Kimitsu Chuo Hospital.

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