Development and validation of the 22-item Tarumi’s Modern-Type Depression Trait Scale: Avoidance of Social Roles, Complaint, and Low Self-Esteem (TACS-22)

Takahiro A. Kato, MD, PhD,†,‡,§,†† Ryoko Katsuki, MA,†† Hiroaki Kubo, MA,† Norhiro Shimokawa, MD,† Mina Sato-Kasai, MD,† Kohei Hayakawa, MD,† Nobuki Kuwano, MD,† Wakako Umene-Nakano, MD, PhD,† Masaru Tateno, MD, PhD,∥,‡‡ Daiki Setoyama, PhD,∥ Dongchon Kang, MD, PhD,∥ Motoki Watabe, PhD,∥ Shinji Sakamoto, PhD,∥ Alan R. Teo, MD, MS,∥,††† Takahiro A. Kato, MD, PhD

Aim: Understanding premorbid personality is important, especially when considering treatment selection. Historically, the premorbid personality of patients with major depression in Japan was described as _Shuchaku-kishitsu_ [similar to Typus melancholicus], as proposed by Shimoda in the 1930s. Since around 2000, there have been increased reports in Japan of young adults with depression who have had premorbid personality differing from the traditional type. In 2005, Tarumi termed this novel condition ‘dysthymic-type depression,’ and more recently the condition has been called _Shin-gata/Gendai-gata Utsu-byo_ [modern-type depression (MTD)]. We recently developed a semi-structured diagnostic interview to evaluate MTD. Development of a tool that enables understanding of premorbid personality in a short time, especially at the early stage of treatment, is desirable. The object of this study was to develop a self-report scale to evaluate the traits of MTD, and to assess the scale’s psychometric properties, diagnostic accuracy, and biological validity.

Methods: A sample of 340 participants from clinical and community settings completed measures. Psychometric properties were assessed with factor analysis. Diagnostic accuracy of the MTD traits was compared against a semi-structured interview.

Results: The questionnaire contained 22 items across three subscales, thus we termed it the 22-item Tarumi’s Modern-Type Depression Trait Scale: Avoidance of Social Roles, Complaint, and Low Self-Esteem (TACS-22). Internal consistency, test–retest reliability, and convergent validity were all satisfactory. Among patients with major depression, the area under the curve was 0.757 (sensitivity of 63.1% and specificity of 82.9%) and the score was positively correlated with plasma tryptophan.

Conclusion: The TACS-22 possessed adequate psychometric properties and diagnostic accuracy in an initial sample of Japanese adults. Additional research on its ability to support clinical assessment of MTD is warranted.

Keywords: dysthmic-type depression, hikikomori, major depressive disorder, melancholic-type depression, premorbid personality.

Understanding the premorbid personality of depression patients is important, especially when considering treatment selection. Historically, the premorbid personality of patients with major depression in Japan was described as _Shuchaku-kishitsu_ [similar to Typus melancholicus], as proposed by Shimoda in the 1930s. This kind of personality is characterized by traits such as diligence, deep sincerity, and perfectionism. _Shuchaku-kishitsu_ has many points in common with melancholic temperament, which was proposed by Tellenbach in Germany in 1961. Since the 1970s, different types of depression with different premorbid personality types have been reported among young people by Japanese psychiatrists; for example, _Taikyaku shinketsu-sho_ [withdrawal neurosis], _Tohi-gata utsu-byo_ [avoidant type of depression], _Gendai-gata utsu-byo_ [modern type of depression], and _Mizyuku-gata utsu-byo_ [immature type of depression]. Especially since around 2000, there have been increased reports in Japan of young adults with depression who have had...
premorbid personality differing from the traditional type. In 2005, Tarumi termed this novel condition ‘dysthymic-type depression’ in contrast to the melancholic-type depression proposed by Shimoda, and Tarumi also proposed its premorbid personality.10,11 This syndrome is currently called Shin-gata/Gendai-gata utsu-byo (new-type depression or modern-type depression (MTD)) and is characterized by a tendency for the presentation of depressive symptoms mainly in stressful workplace or school settings, with the rapid decrease or disappearance of these symptoms once patients leave these stressful situations.12–16

Tarumi pointed out that the premorbid personality and symptomatological characteristics of MTD include avoidant narcissistic personality (‘attachment to himself/herself without roles,’ ‘negative feeling about social order,’ and ‘vague omnipotent thoughts’), extrapunitive feeling (‘criticism of others’), and stress related to social norms, including social rules and social expectations.10,11 Based on Tarumi’s notes, we temporarily developed our original diagnostic criteria of MTD and a semi-structured diagnostic interview to evaluate the condition.14 Our proposed diagnostic criteria for MTD include the following items (details are shown in Kato et al.14): (i) an overt appeal of depressive mood, which is based on a belief that the individual him/herself is clinically depressed; (ii) expressing a desire to be excused or spared from duties or responsibilities (e.g., school, work) because of ‘depression’ (i.e., the individual’s overall functioning worsens during work or school, whereas it is maintained relatively higher at other times); and (iii) traits (including premorbid personality, behavioral pattern, and interpersonal pattern) such as ‘never has been diligent,’ ‘an avoidance/hatred of hierarchies and ranks in society,’ ‘a preference to exist without social roles,’ ‘an omnipotent type,’ and ‘a vague sense of omnipotence.’

We define a person who has three or more of these final five factors as having MTD traits. However, having MTD traits is not equated with a clinically diagnosed case of MTD. We define the individual who meets all of the above items (i, ii, and iii) as diagnosed with MTD. We have proposed that a ‘typical’ case of MTD does not meet the full criteria for major depressive disorder (MDD). On the other hand, MTD patients who meet the full criteria for MDD also exist, at least in our clinical practice. Thus, we are also proposing to name such cases as ‘severe’ cases of MTD.

Tarumi proposed a possibility of differences in therapeutic response and prognosis by medical treatment between traditional melancholic-type depression and MTD.10,11 which has been increasingly reported in current clinical practice in Japan.13,14,16 Tarumi noted that drug responses to antidepressants are better among patients with traditional melancholic-type depression compared to those with MTD, and that antidepressants tend to worsen the prognosis of MTD.10,11 We have recently proposed that psychosocial interventions (e.g., environmental regulation, group psychotherapy) should be primarily considered in the treatment strategies of typical cases of MTD, as unwarranted medication can prolong or worsen the condition and therefore requires caution. In severe cases of MTD, psychosocial interventions (e.g., environmental regulation, group psychotherapy) should be considered first, and depending on the severity of the depressive condition, pharmacological intervention (e.g., antidepressants) should be considered.

Now we are faced with the important task of distinguishing these clinical conditions in the clinical practice of treating depression.13–18 In MTD evaluation, it is important to understand the traits, especially premorbid personality as proposed by Tarumi.10,11,13,14 However, in daily clinical practice there is not a lot of time to spare for understanding a patient’s premorbid personality in medical interviews. Development of a tool that enables a quick understanding of a patient’s premorbid personality at the early stage of treatment, especially before therapeutic intervention, is desirable. Considering such a background, we herein established a self-report scale to facilitate evaluation of the traits (including premorbid personality) of MTD proposed by Tarumi10,11 and assessed the scale’s psychometric properties and diagnostic accuracy in clinical and community samples. Finally, we analyzed a pilot biological validity of the scale using a blood biomarker dataset.

Methods

All methods of this study were performed in accordance with the Declaration of Helsinki and were approved by the ethics committees of Kyushu University, Fukuoka, Japan.

Phase 1: Item pool development

In this study, we prepared question items based on the premorbid personality and symptomatological characteristics of MTD, which were shown in Tarumi and Kanba.10,11 Kato et al. arranged the premorbid personality and symptomatological characteristics of MTD shown by Tarumi et al. into the temperament, premorbid personality, and behavioral tendency of MTD.14 Based on this, we compiled the contents into items as follows: vague omnipotent thoughts, avoidance tendency, attachment to him/herself without social roles, resistance against social order because of stress, not being so energetic in work by nature, and hatred and avoidance of a hierarchical-type society. In addition to those ideas, considering psychological scales to assess severity of depression and anxiety, personality tendency, and also characteristics of patients seen in actual clinical practice, we extracted texts representing traits of MTD. Following review by clinicians (psychiatrists and clinical psychotherapists), we finally prepared 71 question items.

Phase 2: Data collection

Recruitment

Study recruitment occurred in Fukuoka, a major metropolitan area in southern Japan. All participants provided written informed consent and received a gift card incentive worth approximately $18.

As a clinical sample, a total of 238 patients (130 males and 108 females) who visited the Kyushu University Hospital and affiliated medical institutions were recruited. The mean age was 34.11 years (SD, 8.44 years; range, 18–50 years). As a community sample, a total of 102 volunteers (46 males and 56 females) were also recruited at Kyushu University via posters and flyers seeking ‘healthy volunteers.’ The mean age of the volunteers was 23.03 years (SD, 5.37 years; range, 19–48 years). Exclusion criteria included: age < 15 years or >50 years; inability to understand written Japanese; a self-reported history of schizophrenia; or severe heart, liver, or kidney disease. Data were collected between May 2014 and May 2017.

Procedure

All the participants agreed to cooperate in this research. We applied the self-report questionnaire consisting of 71 items representing MTD traits to 238 patients. Answers were rated on a 5-point scale as 0 (Disagree), 1 (Somewhat disagree), 2 (Neither agree nor disagree), 3 (Somewhat agree), and 4 (Agree). In addition, 102 healthy participants were administered a test–retest investigation. They took the same questionnaire twice within a 2-week interval to assess the reliability by the test–retest method. To examine the convergent validity of the scale we had developed, we conducted an existing diagnostic assessment of MTD and administered related psychological scales in the 238 patients.

Diagnostic evaluation of MTD

We originally established a semi-structured diagnostic interviewing system to assess MTD, including the traits of MTD.14 Using this system, we assessed the extent to which participants had the traits of MTD (including premorbid personality, behavioral pattern, and interpersonal pattern) on a scale from 1 (Not at all) to 10 (Typical case) based on the contents of life history and current medical history obtained from participants during their interview, their behavior during the interview, and opinions from others (family members and/or colleagues). Tentative scores were calculated by a discussion between a psychiatrist and a clinical psychotherapist who had met participants directly, based on these scores, a consensus meeting was held involving the other psychiatrists and clinical psychotherapists to determine the final scores. At this point, the
In this study, numbers for an item as points of each subscale. Kasahara’s Inventory for the Melancholic-Type Personality
We used Kasahara’s Inventory for the Melancholic-Type Personality to investigate a relation between our trait scale and the premorbid personality of patients with traditional melancholic-type depression. Kasahara’s Inventory is a self-rated scale to measure the premorbid personality of patients with melancholic-type depression where 15 items about attitudes ‘when participants are healthy’ are rated on a 2-point scale of 1 (Yes) and 0 (No) based on the test method of Sato et al.19

Structured Clinical Interview for DSM-IV-TR Axis I Disorders
MDD was diagnosed using the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I).20

Structured Clinical Interview for DSM-IV Axis II Personality Disorders Personality Questionnaire
The Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) is a semi-structured interview for assessment of 10 Axis II personality disorders and an additional two personality disorders (depressive personality disorder and passive-aggressive personality disorder) based on the DSM-IV.21,22 A self-reporting SCID-II Personality Questionnaire has been developed for screening.21,23 We used this questionnaire to investigate a relation between our trait scale and personality tendency, especially for narcissistic and avoidant tendencies. Among a total of 119 items of the SCID-II Personality Questionnaire, in this study we used a 17-item subscale relating to narcissistic personality disorder and a 7-item subscale relating to avoidant personality disorder. Each subscale was measured on a 2-point scale of 1 (Yes) and 0 (No) where we considered the relevant numbers for an item as points of each subscale.

Temperament and Character Inventory – Revised, 140-item Japanese version
Furthermore, we investigated a relation between our trait scale and personality tendency based on the 7-factor biosocial model by Cloninger et al.24,25 Cloninger et al. proposed the description of a personality tendency according to four temperament factors (Novelty Seeking, Harm Avoidance, Reward Dependence, and Persistence) that are biological and genetic causes and according to three personality factors (Self-Directedness, Cooperativeness, and Self-Transcendence) that are impacted more significantly by environment.24 In this study, using the Temperament and Character Inventory – Revised, 140-item (TCI-140) Japanese version,26 we obtained answers on a 5-point scale ranging from 0 (Definitely false) to 4 (Definitely true).

Next, to investigate a relation between our trait scale and the severity of depression and the levels of anxiety, we used the following three scales.

Patient Health Questionnaire-9
A self-report questionnaire, the Patient Health Questionnaire (PHQ)-9, was developed to make an assessment of severity of depression in a short time based on nine items excerpted from the module of MDD in the DSM-IV.27 In this study, we used the PHQ-9 Japanese Version.28 The PHQ-9 is a scale to measure depressive symptoms during the past 2 weeks. Answers on nine items relating to symptoms were given on a 4-point scale from 0 (Not at all) to 3 (Nearly every day).

Beck Depression Inventory – Second Edition
The Beck Depression Inventory – Second Edition (BDI-II) is one of the most reliable self-rated scales to assess severity of depression and was amended in adherence with the DSM-IV.29 We used the Japanese version of the BDI-II30 Answers to a total of 21 items were given on a 4-point scale. Participants selected the answers that most closely described the way they had been feeling during the past 2 weeks, including that day.

State–Trait Anxiety Inventory
The State–Trait Anxiety Inventory (STAI) assesses anxiety from two aspects: state anxiety and trait anxiety.31 The STAI Japanese Version32 consists of 40 items: 20 measuring state anxiety and 20 measuring trait anxiety. Answers were given on 4-point scales for state anxiety ranging from 0 (Not at all) to 3 (Very much so) and for trait anxiety ranging from 0 (Almost never) to 3 (Almost always).

Phase 3: Statistical analysis
All analyses were performed using IBM SPSS 24 Advanced Statistics for Mac OS.

The first step involved selection of question items and was conducted using the clinical sample data (238 patients). Factor analysis with the maximum likelihood method and the promax rotation was performed to explore factor structure of the developed scale and to improve its validity excluding less related items. In the second step, Pearson correlation was conducted to assess convergent validity. Cronbach’s alpha coefficient was used to evaluate internal consistency. For assessing test–retest reliability, we calculated Pearson correlation coefficients using community sample data (102 participants). For the third step, receiver–operator characteristic (ROC) analysis was performed with the clinical sample data to assess the diagnostic consistency of our trait scale. Finally, for the fourth step, to investigate biological validity of personality traits measured in the developed scale, we conducted Spearman rank correlation and Mann–Whitney U-test using data of 19 drug-free patients with MDD. In this study, P-values of <0.05 were considered as statistically significant, and P-values of <0.1 were considered as marginally significant.

First step: Selection of question items
Initially, we screened items for variability, violation of normality assumptions, and poor reliability. We first calculated skewness of 71 items for which answers were obtained. An item ranked in the 66th percentile or higher among all items was considered as a candidate for exclusion. We also calculated the mean value of 71 items. An item ranked in the 90th percentile or higher or in the 10th percentile or lower was considered as a candidate for exclusion. Next, among the residual items, when an item had a corrected item–total correlation of below 0.31, we considered the item as a candidate for exclusion.

Muranaka et al. pointed out three problems occurring when items for a self-assessment scale are prepared based on characteristics observed by a third person.33 The three points were as follows: (i) when items describing characteristics based on assessment results by others are prepared, the concrete contents would become obscure; (ii) as psychopathological characteristics summarized as assessment by others are not deeply involved in the performer’s mentality, it is difficult to gain insight into the self-relating judgment for the characteristics; and (iii) the scale includes items other than personality characteristics. Considering these points, we decided to exclude some items.

Subsequently, we conducted an exploratory factor analysis with the maximum likelihood method and the promax rotation on the remaining 22 candidate items. The three factors were extracted based on scree plot and factor loading.

Second step: Verification of reliability and validity
We computed Cronbach’s alpha coefficients to measure internal consistency of each factor. To assess test–retest reliability, we calculated Pearson correlation coefficients between the scores of the developed scale on two time periods. As an assessment of convergent validity, Pearson correlation coefficients were computed between the developed scale and related psychological scales.
Third step: ROC analysis
In this study, we tried to determine a potential cut-off score for the
developed scale to distinguish individuals if a participant had a cer-
tain level of the traits of MTD, using scores of the semi-structured
diagnostic interview of MTD, which we have developed.4 By mutual
consultation, we considered cases with an interview-based assessment
score of six or higher as the MTD traits high-score group and cases
with a score of five or lower as the MTD traits low-score group.
We evaluated the diagnostic accuracy of the developed scale
across multiple cut-off scores using multiple measures: sensitivity
(percentage of the MTD traits high-score group cases correctly identi-
fied), specificity (percentage of the MTD traits low-score group cases
correctly identified), positive likelihood ratio (LR+, ratio of true posi-
tives to false positives), negative likelihood ratio (LR−, ratio of true
negatives to false negatives), positive predictive value (PPV, probabili-
ity of a positive test result being a true positive), negative predictive
value (NPV, probability of negative test result being a true negative),
and area under the ROC curve. In order to calculate PPV and NPV,
we assumed a sample prevalence of 22.5% for the MTD traits high-
score group. In addition, to evaluate the diagnostic accuracy of the
MTD traits among patients with MDD, we conducted ROC using data
of 68 patients with MDD among a clinical sample, who were diag-
nosed based on SCID-I.
In this study, the area under the curve (AUC) provides the possi-
bility to correctly distinguish whether randomly sampled participants
have the MTD traits score of not less than six. Assuming that a value
of 0.5 can distinguish it by chance, an AUC of 0.7 or higher is con-
sidered to be moderately likely to distinguish it.

Fourth step: Pilot analysis of biological validity
Despite the gradual clarification of the biological aspects of
depression,4 the biological basis of depression-related personality
traits has not been well clarified. Tryptophan metabolites, especially
serotonin, have gathered greater attention in the endeavor to under-
stand the pathophysiology of depression.4 In addition, metabolites
of the tryptophan–kynurenine pathway are increasingly attracting
interest.4 Just recently, we reported that plasma tryptophan is a
possible diagnostic biomarker of MDD and that some of the
tryptophan–kynurenine metabolites in plasma are related to severity
of some depressive symptoms.49 We recently reported that the levels
of plasma tryptophan and kynurenine are lower in MDD patients
compared to healthy controls, and that especially lower levels of
plasma tryptophan are a diagnostic biomarker of MDD.49 Using
Kuwano et al’s blood biomarker dataset (as a secondary-use),49 we
preliminarily tried to investigate the biological validity of personality
traits of two different types of depression: MTD and traditional
melancholic-type depression among MDD patients. We used the pre-
viously reported plasma concentration data of serotonin and
tryptophan–kynurenine metabolites, including tryptophan,
kynurenine, and kynurenic acid measured by liquid chromatography–
mass spectrometry using LSMS-8040 (Shimadzu, Kyoto, Japan).49
To evaluate relations among the blood metabolites and depression-
related personality traits, we calculated Spearman rank correlation
coefficients between the concentrations of blood metabolites, TACS-
22 scores, and Kasahara’s Inventory scores among 19 drug-free
patients with MDD. In addition, the Mann–Whitney U-test was per-
formed for comparison.

Results
Factor structure and reliability
Based on the first-step statistical analysis (selection of question items)
using the clinical samples (238 patients, including 67 patients who
met the diagnostic criteria of MDD), 22 items were extracted. To
investigate the factor structure of the scale, we conducted an explor-
atory factor analysis using the 22 items of remaining candidates. In a
factor analysis with the maximum likelihood method, eigenvalues
were 1.0 or higher for up to the fifth factors while eigenvalues had
smaller changes for the fourth or previous factors. Thus, we decided
to extract the upper three factors. Finally, a total of 22 items were
fixed (Table 1). The obtained results were generally consistent with
both the purpose of preparing scales (i.e., assessment of the
premorbid personality of MTD) and the idea proposed as a hypothe-
sis. Based on the contents of items, factors were termed ‘Avoidance
of Social Roles,’ ‘Low Self-Esteem,’ and ‘Complaint.’
Next, we calculated Cronbach’s alpha coefficients by overall
scale and by factor to assess the internal consistency of each factor.
The following values were obtained: the overall scale = 0.80, Factor 1 (Avoidance of Social Roles) = 0.74, Factor 2 (Low Self-Esteem)
= 0.64, Factor 3 (Complaint) = 0.75.

Test–retest reliability
We performed the test–retest investigation in 102 healthy participants
to assess the reliability. The Pearson correlation coefficient was calcu-
lated by points of the scale. As a result, r = 0.69 (P < 0.001) for
points of the first factor, Avoidance of Social Roles; r = 0.78
(P < 0.001) for points of the second factor, Low Self-Esteem; and
r = 0.76 (P < 0.001) for points of the third factor, Complaint. This
shows sufficient test–retest reliability for each point.

From the above results, we concluded that the factorial validity
and reliability of 22 items used in this study were generally preserved.
We titled the original self-report questionnaire using these 22 items
the ‘22-item Tarumi’s Modern-Type Depression Trait Scale: Avoid-
ce of Social Roles, Complaint, and Low Self-Esteem.’ Hereinafter,
our trait scale is referred to using its abbreviation, the TACS-22.

Convergent validity
The correlations shown in Table 2 are among and between the follow-
ing: Kasahara’s Inventory, the SCID-II Personality Questionnaire
(Narcissistic Personality Disorder and Avoidant Personality Disorder),
the TCI-140, the PHQ-9, the BDI-II, the Trait/State anxiety levels of
the STAI, and the TACS-22. As we expected, the total scores of the TACS-22 had significant positive relations with subscales in the
SCID-II – Narcissistic Personality Disorder (r = 0.454, P < 0.001)
and Avoidant Personality Disorder (r = 0.472, P < 0.001) – and Harm
Avoidance in the TCI-140 (r = 0.495, P < 0.001). Likewise, the total
score of the TACS-22 had a significant positive relation with the
scales related to anxiety and depression: State in the STAI (r = 0.364,
P < 0.001), Trait in the STAI (r = 0.548, P < 0.001), the BDI-II
(r = 0.43, P < 0.001), and the PHQ-9 (r = 0.335, P < 0.001).
In addition, we analyzed the relations between each subscale of
the TACS-22 and the above scales as follows.

Using Kasahara’s Inventory, we investigated the relation between
each of the subscales and the premorbid personality of traditional
melancholic-type depression. Correlation analysis revealed no signifi-
cant relations with the first factor, Avoidance of Social Roles, or with
the third factor, Complaint. On the other hand, a weak but significant
positive relation was observed with the second factor, Low Self-
Esteem (r = 0.237, P < 0.001).

The correlations between the score relating to Narcissistic Per-
sonality Disorder in the SCID-II Personality Questionnaire and each
of the subordinate factors showed weak to medium relations
(r = 0.252 to 0.385, P < 0.001). The correlations between the score
relating to avoidant personality disorder and each of the subordinate
factors showed weak to medium relations (r = 0.286 to 0.433,
P < 0.001).
TCSI-140 factors were shown to have significantly positive and/or
negative relations with some of the three TACS-22 subscales. Espe-
cially, Harm Avoidance, Self-Directedness, and Cooperativeness were
shown to have moderately to highly significant relations with all three
factors. The first factor, Avoidance of Social Roles, was significantly
correlated with almost all factors of the TCI-140 except Self-
Transcendence.
For the relation with the severity of depression, we used the
PHQ-9 and BDI-II. In the PHQ-9, there were weak correlations with
We determined cases with the interview-based assessment of the second factor, Low Self-Esteem, and the third factor, Complaint ($r = 0.351$ to $0.442$, $P < 0.001$), similarly in the BDI-II, there were relatively strong correlations with the second factor, Low Self-Esteem, and the third factor, Complaint ($r = 0.422$ to $0.567$, $P < 0.001$).

In STAI-Trait, regarding the levels of anxiety, there were relatively weak to relatively strong significant relations with each factor ($r = 0.222$ to $0.605$, $P \leq 0.001$). In STAI-State, there was also a weak correlation with the second factor, Low Self-Esteem, and the third factor, Complaint ($r = 0.351$ to $0.447$, $P < 0.001$).

### Diagnostic accuracy

We conducted ROC analysis to investigate distinguishability using the TACS-22. The AUC, which indicates a comprehensive diagnostic accuracy of TACS-22, was 0.721 (Fig. 1).

To determine a potential cut-off score for the TACS-22 to distinguish if a participant had a certain level of the MTD traits, we compared distinguishing rates using the TACS-22 score and an interview-based assessment score (1–10) that we originally developed. We determined cases with the interview-based assessment score of six or higher as the MTD traits high-score group and cases with the score of five or lower as the MTD traits low-score group, based on which we searched for the cut-off value that could provide the highest distinguishing rate for these two groups. The results are shown in Table 3. When we distinguished clinical patients who participated in this study ($N = 238$), a cut-off score of 48 (out of a possible 88 points) provided a sensitivity of 71.2%, a specificity of 62%, a PPV of 35.2%, and an LR+ of 1.87. A cut-off score of 49 provided a slightly decreased sensitivity of 59.6% with no clear changes in specificity, PPV, or LR+ (shown in Table 4).

Furthermore, when we tried to distinguish 67 patients who met the diagnostic criteria of MDD among the clinical samples, the AUC increased to 0.757. A cut-off score of 54 (based on a maximum of 88) provided a sensitivity of 63.1%, a specificity of 82.9%, a PPV of 0.6, and an LR+ of 3.71.

We also conducted a preliminary biological validation using the blood biomarkers from drug-free patients with MDD ($N = 19$). As shown in Table S1, there was a marginally positive correlation between tryptophan and the total score of TACS-22 ($r = 0.433$, $P = 0.064$). Interestingly, tryptophan was significantly positively correlated with the TACS-22 Complaint subscale score ($r = 0.521$, $P = 0.022$). On the other hand, the total score of Kasahara's Inventory had a significant positive correlation with serotonin ($r = 0.515$, $P = 0.024$). Kasahara's Inventory was significantly negatively correlated with kynurenic acid/kynurenine ($r = -0.534$, $P = 0.018$). The results are shown in Table S1.

Based on the ROC analysis, a potential cut-off TACS-22 score among MDD patients is 54. Thus, 19 drug-free patients with MDD were divided into two groups: MDD patients who showed a total score of greater than 54 as the TACS-22 high group ($N = 3$) and MDD patients who showed the total score of 53 or less as the TACS-22 low group ($N = 16$). We compared the levels of blood metabolites between the two groups using the Mann–Whitney U-test (Table S2). Tryptophan was significantly greater in the TACS-22 high group (Mdn = 16.328) compared to the TACS-22 low group (Mdn = 12.582) ($U = 2$, $P = 0.008$). On the other hand, no significant difference was found in serotonin between the two groups.

### Discussion

In this study, we developed an original self-report questionnaire named the ‘22-item Tarumi’s Modern-Type Depression Trait Scale: Avoidance of Social Roles, Complaint, and Low Self-Esteem (TACS-22),’ which can evaluate the premorbid personality of Tarumi’s dysthymic-type depression or MTD. We assessed the validity and reliability of the TACS-22 using the data of clinical and community samples. Subsequently, using data actually obtained from clinical patients, we verified the distinguishability.

Three factors (Avoidance of Social Roles, Low Self-Esteem, and Complaint) were extracted from the TACS-22 through an exploratory factor analysis. Correlation analysis between the three factors of the TACS-22 and other psychometric scales suggests some interesting relations. We hypothesized that the premorbid personalities between MTD and traditional melancholic-type depression are directed oppositely. However, a positive correlation was observed between the TACS-22 Low Self-Esteem and the total score of Kasahara’s...
In Receiver type depression. On the other hand, the other two TACS-22 factors, that low self-esteem is the common factor for MTD and melancholic-type depression. 6,19,50 This study indicates Inventory, which is an indicator about the premorbid personality of modern-type depression (MTD; N = 238). Area under the ROC = 0.721.

Table 2. Correlations between TACS-22 scores and related psychological scales

| Scale                                         | N   | Mean  | SD   | TACS-22 total | Avoidance of Social Roles | Low Self-Esteem | Complaint |
|-----------------------------------------------|-----|-------|------|---------------|---------------------------|-----------------|-----------|
| TACS-22 Total                                 | 234 | 46.77 | 11.59| —             | 0.766**                   | 0.63**          | 0.785**   |
| Avoidance of Social Roles                     | 217 | 6.54  | —    | —             | —                         | 0.143**         | 0.349**   |
| Low Self-Esteem                               | 153 | 4.22  | —    | —             | —                         | —               | 0.430**   |
| Complaint                                     | 96  | 5.01  | —    | —             | —                         | —               | —         |
| Kasahara’s Inventory for the Melancholic-Type Personality | 231 | 10.91 | 2.62 | 0.03          | 0.10                      | 0.237**         | 0.00      |
| SCID-II                                      | 233 | 10.91 | 2.62 | 0.03          | 0.10                      | 0.237**         | 0.00      |
| Narcissistic Personality Disorder             | 3   | 2.76  | 0.454**| 0.349**          | 0.252**                   | 0.385**         |
| Avoidant Personality Disorder                 | 4   | 2.04  | 0.472**| 0.286**         | 0.433**                   | 0.356**         |
| TCI-140                                      | 228 |       |      |               |                           |                 |           |
| Novelty Seeking                               | 57  | 8.22  | 0.092| 0.169*        | −0.10                     | 0.07            |
| Harm Avoidance                                | 75  | 12.20 | 0.495**| 0.302**         | 0.539**                   | 0.302**         |
| Reward Dependence                             | 62  | 9.69  | −0.298**| −0.215**       | −0.199**                  | −0.243**        |
| Persistence                                   | 57  | 13.06 | −0.241**| −0.381**       | 0.00                      | −0.06           |
| Self-Directedness                             | 54  | 12.15 | −0.652**| −0.387**       | −0.596**                  | −0.0509**       |
| Cooperativeness                               | 67  | 9.07  | −0.468**| −0.381**       | −0.212**                  | −0.414**        |
| Self-Transcendence                            | 33  | 8.60  | 0.123| 0.05          | 0.08                      | 0.155*          |
| PHQ-9                                         | 234 | 12.82 | 0.335**| 0.09          | 0.368**                   | 0.351**         |
| BDI-II                                        | 233 | 12.79 | 0.43**| 0.06          | 0.567**                   | 0.442**         |
| STAI                                           | 232 |       |      |               |                           |                 |           |
| Trait                                          | 57  | 11.90 | 0.548**| 0.222*        | 0.605**                   | 0.470**         |
| State                                          | 54  | 11.80 | 0.364**| 0.09          | 0.447**                   | 0.351**         |

Statistical P-values were derived from Pearson correlation analysis.

*P < 0.05.
**P < 0.01.

BDI-II, Beck Depression Inventory-Second Edition; PHQ-9, Patient Health Questionnaire-9; SCID-II, Structured Clinical Interview for DSM-IV Axis II Personality Disorders; STAI, State–Trait Anxiety Inventory; TACS-22, Tarumi’s Modern-Type Depression Trait Scale: Avoidance of Social Roles, Complaint, and Low Self-Esteem; TCI-140, 140-item Temperament and Character Inventory Revised.

Avoidance of Social Roles and Complaint, did not show significant correlation with Kasahara’s Inventory. Low Self-Esteem is just one of three factors in the TACS-22; therefore Avoidance of Social Roles and Complaint may contribute to distinguishing between MTD and melancholic-type depression. As for the blood biomarker data, tryptophan showed significant positive correlation to the TACS-22 Complaint, but none of the blood metabolites showed a significant correlation to Low Self-Esteem. In addition, serotonin was significantly positively correlated with Kasahara’s Inventory but showed no significant correlation to the TACS-22. Therefore, our results suggest that at least partial biological differences exist between the traits of MTD and melancholic-type depression.

In addition, this study suggests that depression and anxiety severity, assessed by the PHQ-9, BDI-II, and STAI, were significantly correlated with the Low Self-Esteem score. Generally, the Japanese have lower self-esteem compared to people in other countries.51 In the TACS-22, Low Self-Esteem includes several items, such as ‘I am a vulnerable person’ and ‘I think somehow life will turn out okay (reverse-scored item),’ indicating poor self-efficacy, which is an individual’s belief in his/her ability to regulate his/her environment according to the objectives and change the situation toward the desired direction. Future interventional approach to enhance self-esteem is highly expected in the clinical practice and prevention of depression, regardless of the types of premorbid personality, at least in Japan.

All three factors were positively correlated with both Narcissistic and Avoidant Personality Tendencies in the SCID-II. Especially, Low Self-Esteem was shown to have high levels of relation with Avoidant Personality Tendency. Avoidant personality is suggested to be linked to hikikomori, a severe form of social withdrawal syndrome, originally
Future studies are warranted to clarify the interaction between the TACS-22 and HQ-25 as those that could be impacted by the environment. We also propose that directness and cooperativeness are acquired characteristics as “receiving greater impact by environment.” In other words, we can regard the concepts assessed by the TACS-22 as those that could be impacted by the environment and that include plasticity rather than as innate factors. This finding could reflect the fact that the common age for MTD is described as adolescence and early adulthood (20s to 30s). The TACS-22 may be an indicator that captures personality tendencies that are changeable depending on experience with advancing years. Further longitudinal studies are needed to clarify these aspects.

As a scale similar to the TACS-22, Muranaka et al. developed an indicator Interpersonal Sensitivity/Privileged Self Scale (hereinafter referred to as IPS Scale), which expresses the psychological characteristics of Shin-gata utsu-byo [new-type depression]. The IPS Scale is a questionnaire developed by adding characteristics of Mizukaga-gata utsu-byo [innate type of depression] and Gendai-gata utsu-byo [modern type of depression] to characteristics of Tarumi’s dysphoric-type depression. The TACS-22 is similar to the IPS Scale, especially in the Privileged-Self factor. The IPS Scale was developed among college students (community samples), while the TACS-22 was developed among patients with psychiatric disorders, including patients with depression (clinical samples), which is the main difference. It is expected that investigations will make progress concerning use of and needs for both scales by conducting surveys using both scales in the same participants, including psychiatric patients.

This study indicates that the TACS-22 total score can relatively well extract patients with the premorbid personality of MTD from clinical samples. Especially, in a group of patients with MDD, the distinction using the TACS-22 provided a specificity of 82.9%, which indicates a high possibility to exclude those without many features of the premorbid personality of MTD. This result suggests that the TACS-22 can be an important tool when evaluating and selecting treatments for patients with depressive symptoms. As limited empirical research has been conducted regarding MTD, the TACS-22 has potential for application in clinical research settings, such as comparisons of therapeutic effects among several treatments depending on the TACS-22 score.

Plasma tryptophan showed marginally positive correlation with the total score of the TACS-22 and significantly positive correlation with the TACS-22 Complaint subscale score. The total score of Kasahara’s Inventory, a trait scale of melancholic-type depression, was positively correlated with plasma serotonin, and also negatively correlated with the ratio of kynurenic acid/kynurenine. Our pilot analysis using the secondary-use MDD blood biomarker data indicated that different biological mechanisms may exist between the traits of MTD and traditional melancholic-type depression. Further clinical neuroscience investigations using the TACS-22 are expected to reveal a deeper biological basis of MTD.

Several previous studies have shown reduction of plasma tryptophan among MDD patients. Interestingly, in the present pilot analysis, plasma tryptophan was significantly greater in the TACS-22 high group compared to the TACS-22 low group among 19 drug-free MDD patients. Our results indicate that plasma tryptophan may be high (definitely not low) among MTD patients who are diagnosed with MDD. However, this sample size was small, and additional evaluations with greater sample sizes should be conducted.

Similar to the hikikomori scale, HQ-25, a full version of the TACS-22 is freely available, which is presented in Table S3. To facilitate broader evaluation and use in other populations, we present an English version. This was developed using independent translation by two bilingual individuals with backgrounds in clinical psychology, with adjudication of discrepancies by the authors, T. A. K. and A. R. T.

The present study has some limitations. The main limitation is the small sample size. Second, in the biomarker analysis, we did not use multiple test correction to avoid the risk of false negatives, as the purpose of this investigation was to serve exploratory research.
pilot outcomes. Further studies with greater sample sizes should be conducted to evaluate the validity of the TACS-22 and our preliminary findings on the blood biomarker among patients with MDD.

**Conclusion**

In this study, we developed a self-report scale, the TACS-22, to assess the traits of Tarumi’s dysthymic-type depression or MTD using tentative small Japanese clinical and community samples. It is strongly desired to conduct further validity assessments of the scales by adding other cohorts and larger sample sizes.

This scale can be expected to have large significance for the progress of practical studies of MTD. Especially, considering that this scale is expected to make it possible to distinguish MTD from traditional melancholic-type depression, assessing validity of the scale in samples including a larger number of MTD patients is an issue in the future. Patients with MTD seem to exist not only in Japan but also other countries, thus international studies using TACS-22 should be conducted.

We believe that further practical use of the TACS-22 in psychiatry, psychology, primary care, and community fields will help to clarify the occurrence of MTD and its biopsychosocial mechanisms in future.

**Acknowledgments**

A series of MTD studies in Kyushu University have been conducted in accordance with the cherished desire of the late Dr Shin Tarumi (1971–2005). The authors would like to thank Dr Koji Tanaka, Dr Hideki Horikawa, Mr Keita Kurahara, Ms Ayako Inoue, Ms Sakumi Kakimoto, Ms Yoko Zushi, and Ms Keiko Kojima at Kyushu University for their research support and/or assistance. This work was partially supported by a Grant-in-Aid for Scientific Research on: (i) Innovative Areas ‘Will-Dynamics’ of the Ministry of Education, Culture, Sports, Science, and Technology, Japan (JP16H06403 to T.A.K.); (ii) the Japan Agency for Medical Research and Development (AMED) (Syogaisya-Taisaku-Sogo-Kenkyu-Kaihatsu-Jigyo to T.A.K. & S.K. [JP18dk0307075], and Yugo-No to T.A.K. [JP18dm0107095]); (iii) KAKENHI – the Japan Society for the Promotion of Science (JP15K15431 & JP26713039 to T.A.K., and JP16H03741 to S.S. & T.A.K.); (iv) SENSHIN Medical Research Foundation (to T.A.K. and S.K.); and (v) the JSPS Bilateral Joint Research Project between USA and Japan (to T.A.K. and A.R.T). Dr Teo is supported by the Department of Veterans Affairs, and the views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US government. None of the funders had a role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Disclosure statement**

None of the authors report any financial relationships with commercial interests.

**Author contributions**

T.A.K. contributed to the conception and design and was responsible for protocol of the study. T.A.K., R.K., H.K., N.S., M.S-K., K.H., and others contributed to study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Table 5.** The 22-item Tarumi’s Modern-Type Depression Trait Scale (TACS-22): English version

| Item | Disagree | Somewhat disagree | Neither agree nor disagree | Somewhat agree | Agree |
|------|----------|-------------------|--------------------------|---------------|-------|
| 1 I want others around me to tell me it’s okay to take a break. | 0 | 1 | 2 | 3 | 4 |
| 2 I am a vulnerable person. | 0 | 1 | 2 | 3 | 4 |
| 3 I want to spend time only doing things I enjoy rather than working or studying. | 0 | 1 | 2 | 3 | 4 |
| 4 I think somehow life will turn out okay. | 0 | 1 | 2 | 3 | 4 |
| 5 I don’t want to be pressured to fit into conventional social roles. | 0 | 1 | 2 | 3 | 4 |
| 6 I wish I could reset social expectations and rules. | 0 | 1 | 2 | 3 | 4 |
| 7 I want others around me to respect my individuality. | 0 | 1 | 2 | 3 | 4 |
| 8 I am a perfectionist. | 0 | 1 | 2 | 3 | 4 |
| 9 Hardship is necessary in life. | 0 | 1 | 2 | 3 | 4 |
| 10 No one understands me. | 0 | 1 | 2 | 3 | 4 |
| 11 I’d rather go my own way instead of going along with others around me. | 0 | 1 | 2 | 3 | 4 |
| 12 I am unworthy. | 0 | 1 | 2 | 3 | 4 |
| 13 It’s natural to take a break when I am not feeling well. | 0 | 1 | 2 | 3 | 4 |
| 14 I don’t have adequate support from people around me. | 0 | 1 | 2 | 3 | 4 |
| 15 I want to rely on people. | 0 | 1 | 2 | 3 | 4 |
| 16 I feel bad when people are concerned for me. | 0 | 1 | 2 | 3 | 4 |
| 17 I cut corners when I do things I don’t want to do. | 0 | 1 | 2 | 3 | 4 |
| 18 I get blamed for things I didn’t do. | 0 | 1 | 2 | 3 | 4 |
| 19 I don’t want to struggle too much in life. | 0 | 1 | 2 | 3 | 4 |
| 20 I show distress easily through my facial expressions and body language. | 0 | 1 | 2 | 3 | 4 |
| 21 There are many meaningless rules in the world. | 0 | 1 | 2 | 3 | 4 |
| 22 It’s other people’s fault that I am in my current situation. | 0 | 1 | 2 | 3 | 4 |

TACS-22 has a theoretical score range of 0–88.

†Items were reverse-scored.
References

1. Hirschfeld RM, Klerman GL, Lavori P, Keller MB, Griffith P, Coryell W. Premorbid personality assessments of first onset of major depression. Arch. Gen. Psychiatry 1989; 46: 345–345–350.

2. Christensen MV, Kessing LV. Do personality traits predict depression? Acta Psychiatr Scand 1989; 80: 410–414.

3. Shimoda M. Shuchaku-kishitsu ni tsuite. Yonago Med. J. (Yonaga Igaku Zassi) 1950; 2: 1–2 (in Japanese).

4. Shimoda M. On the treatment of involutional depression in my department. Taiwán Igaku Zasshi (Formosa Medicinazhit. J) 1952; 31: 113–115 in Japanese.

5. Tellenbach H. Melancholie. Springer, Berlin, 1961.

6. Kasahara Y, Kimura B. Utsu-byo no rinshoteki-bunrui ni kansuru kenkyu. Seishin Shinkeigaku Zasshi 1975; 77: 715–735 in Japanese.

7. Hirose T. Tohli-gata-uuyo ni tsuite. In: Miyamoto T (ed). Sou-Utsu-Byo no Etsusui-Byori 2 [Psychopathology of Manic-Depressive Illness 2]. Tokyō, 1977; 61–86 in Japanese.

8. Matsunuma K, Yamashita Y. Syakai-Hendo to Utsu-byo; social changes and depression. JPN Bull. Soc. Psychiatry 1991; 14: 193–200 in Japanese.

9. Abe T, Otsuka K, Nagano M, Kato S, Miyamoto T. A consideration on “immature type of depression” : Premorbid personalities and clinical pictures of depression from the structural-dynamic viewpoint (W. Janzarik). JPN Clin. Psychiatr. 1995; 16: 239–248 (in Japanese).

10. Tarumi S, Kanba S. Sociocultural approach toward depression: Dysthymic-type depression. JPN Bull. Soc. Psychiatry 2005; 13: 129–136 in Japanese.

11. Tarumi S. The “new” variant of depression: The dysthymic type. J. Psychiatri Clin. Psychiatry 2005; 34: 687–694 (in Japanese).

12. Kashihara J, Yamakawa I, Kameyama A, Muranaka M, Taku K, Sakamoto S. Perceptions of traditional and modern types of depression: A cross-cultural vignette survey comparing Japanese and American undergraduate students. Psychiatry Clin. Neurosci. 2019; 73: 441–447.

13. Kato TA, Kanba S. Modern-type depression as an ”adjustment” disorder in Japan: The intersection of collectivistic society encountering an individualistic behavior-based system. Am. J. Psychiatry 2017; 174: 1050–1053.

14. Kato TA, Hashimoto R, Hayakawa K et al. Multidimensional anatomy of ‘modern type of depression’ in Japan: A proposal for a different diagnostic approach to depression beyond the DSM-5. Psychiatry Clin. Neurosci. 2016; 70: 7–23.

15. Kato TA, Shinfuku N, Sartorius N, Kanba S. Are Japan’s hikikomori and depression in young people spreading abroad? Lancet 2011; 378: 1070. 

16. Kato TA, Shinfuku N, Fujisawa D et al. Introducing the concept of modern depression in Japan; an international case vignette survey. J. Affect. Disord. 2011; 135: 66–76.

17. Kato TA, Kanba S. Is a socio-cultural analysis of depressive disorders a matter of concern? Response to Kaiya. Am. J. Psychiatry 2018; 175: 483–484.

18. Kato TA, Kanba S. Boundless syndromes in modern society: An interconnected world producing novel psychopathology in the 21st century. Psychiatry Clin. Neurosci. 2016; 70: 1–2.

19. Sato T, Sakado K, Sato D. Differences between two questionnaires for assessment of type melancholicus, Zerssen’s F-list and Kasahara’s scale: The validity and relationship to DSM-III-R personality disorders. Jpn. J. Psychiatry Neurol. 1992; 46: 603–608.

20. First MB, Spitzer RL, Miriam G, Williams JBW. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). American Psychiatric Press, Washington, DC, 1996.

21. First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS. Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II). American Psychiatric Publishing, Washington, DC, 1997.

22. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th edn., Text Revision (DSM-IV-TR). American Psychiatric Publishing, Arlington, VA, 2000.

23. Miller JD, Bagby RM, Pilkonis PA, Reynolds SK, Lynam DR. A simplified technique for scoring DSM-IV personality disorders with the five-factor model. Assessment 2005; 12: 404–415.

24. Cloninger CR, Svrakic DM, Przybeck TR. A psychobiological model of temperament and character. Arch. Gen. Psychiatry 1993; 50: 975–990.

25. Cloninger CR. The Temperament and Character Inventory (TCI): A Guide to its Development and Use. Center for Psychology of Personality, Washington University, St. Louis, MO, 1994.

26. Kojima N, Tanaka E, Suzuki N, Higuchi H, Kitamura T. Reliability and validity of the Japanese version of the Temperament and Character Inventory. Psychol. Rep. 2000; 86: 1050–1058.

27. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. J. Gen. Intern. Med. 2001; 16: 606–613.

28. Muramatsu K, Miyaoaka H, Kamijima K et al. The Patient Health Questionnaire, Japanese version: Validity according to the Mini-International Neuropsychiatric Interview-Plus. Psychol. Rep. 2007; 101: 952–960.

29. Beck AT, Steer RA, Brown GK. Manual for Beck Depression Inventory-Second Edition. Psychological Corporation, San Antonio, TX, 1996.

30. Kojima M, Furukawa TA, Takahashi H, Kawai M, Nagata Y, Tokudome S. Cross-cultural validation of the Beck Depression Inventory-II in Japan. Psychiatry Res. 2002; 110: 291–299.

31. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs G A. Manual for the State-Trait Anxiety Inventory. Consulting Psychologists Press, Palo Alto, CA, 1983.

32. Hidano N, Fukuhara M, Soga S, Spielberger CD. STAI Manual New Edition. Jitsumu Kyoku-Shuppan, Tokyo, 2000.

33. Muranaka M, Yamakawa I, Sakamoto S. Development of the Interpersonal Sensitivity/Privileged Self Scale: The measurement of a psychological characteristic related to “modern-type depression”. Shinchigiku Kenkyu 2017; 87: 622–632 (in Japanese).

34. Kato T, Kanba S. Making psychiatry a clinical neuroscience-based medicine. Psychiatry Clin. Neurosci. 2019; 73: 1.

35. Kunugi H, Hori H, Ogawa S. Biochemical markers subtyping major depressive disorder. Psychiatry Clin. Neurosci. 2015; 69: 597–608.

36. Miller AH, Maletic V, Raison CL. Inflammation and its discontents: The role of cytokines in the pathophysiology of major depression. Biol. Psychiatry 2009; 65: 732–741.

37. Ryff CD, Dienberg Love G, Ury HL et al. Psychological well-being and ill-being: Do they have distinct or mirrored biological correlates? Psychoh. Psychosom. 2006; 75: 85–95.

38. Kato TA, Watabe M, Kanba S. Neuron-glial interaction as a possible glue to translate the mind-brain gap: A novel multi-dimensional approach toward psychology and psychiatry. Front. Psych. 2013; 4: 139.

39. Kondo A, Shoji Y, Morita K et al. Characteristics of oxygenated hemoglobin concentration change during pleasant and unpleasant image-recall tasks in patients with depression: Comparison with healthy subjects. Psychiatry Clin. Neurosci. 2018; 72: 611–622.

40. Jansen R, Penninx BW, Madar V et al. Gene expression in major depressive disorder. Mol. Psychiatry 2016; 21: 339–347.

41. Fava M, Kendler KS. Major depressive disorder. Neuron 2000; 28: 135–341.

42. Oxenkrug G. Serotonin-kynurenine hypothesis of depression: Historical overview and recent developments. Curr. Drug Targets 2013; 14: 514–521.

43. Fakhoury M. Revisiting the serotonin hypothesis: Implications for major depressive disorders. Mol. Neurobiol. 2016; 53: 2778–2786.

44. Cervenka I, Agudelo LZ, Ruas JL. Kynurenines: Tryptophan catabolites (TRYCATs), both of which contribute to the onset of tryptophan and an increased synthesis of detrimental tryptophan metabolites in exercise, in Brain Behav. Immun. 2017; 65: 234–248 (in Japanese).

45. Maes M, Leonard BE, Myint AM, Kubera M, Verkerk R. The new neurocognitive paradigm of depression. Prog. Neuropsychopharmacol. Biol. Psychiatry 2011; 35: 702–721.

46. Setoyama D, Kato TA, Hashimoto R et al. Plasma metabolites predict severity of depression and suicidal ideation in psychiatric patients: A multicenter pilot analysis. PLoS One 2016; 11: e0165267.

47. Dantzer R, Cohen S, Russo SJ, Dinan TG. Resilience and immunity. Brain Behav. Immun. 2018; 74: 28–42.

48. Schwarz R, Stone TW. The kynurenine pathway and the brain: Challenges, controversies and promises. Neuropharmacology 2017; 112: 237–247.
49. Kuwano N, Kato TA, Setoyama D et al. Tryptophan-kynurenine and lipid related metabolites as blood biomarkers for first-episode drug-naive patients with major depressive disorder: An exploratory pilot case-control study. J. Affect. Disord. 2018; 231: 74–82.

50. Furukawa T, Yamada A, Tabuse H et al. Typus melancholicus in light of the five-factor model of personality. Eur. Arch. Psychiatry Clin. Neurosci. 1998; 248: 64–69.

51. Schmitt DP, Allik J. Simultaneous administration of the Rosenberg Self-Esteem Scale in 53 nations: Exploring the universal and culture-specific features of global self-esteem. J. Pers. Soc. Psychol. 2005; 89: 623–642.

52. Kato TA, Kanba S, Teo AR. Hikikomori: Experience in Japan and international relevance. World Psychiatry 2018; 17: 105–106.

53. Kato TA, Kanba S, Teo AR. A 39-year-old "adultolescent": Understanding social withdrawal in Japan. Am. J. Psychiatry 2016; 173: 112–114.

54. Teo AR, Stuflebam K, Saha S et al. Psychopathology associated with social withdrawal: Idiopathic and comorbid presentations. Psychiatry Res. 2015; 228: 182–183.

55. Teo AR, Fetters MD, Stuflebam K et al. Identification of the hikikomori syndrome of social withdrawal: Psychosocial features and treatment preferences in four countries. Int. J. Soc. Psychiatry 2015; 61: 64–72.

56. Kato TA, Tateno M, Shinfuku N et al. Does the 'hikikomori' syndrome of social withdrawal exist outside Japan? A preliminary international investigation. Soc. Psychiatry Psychiatr. Epidemiol. 2012; 47: 1061–1075.

57. Teo AR, Chen JL, Kubo H et al. Development and validation of the 25-item Hikikomori Questionnaire (HQ-25). Psychiatry Clin. Neurosci. 2018; 72: 780–788.

58. Svrakic DM, Draganic S, Hill K, Bayon C, Przybeck TR, Cloninger CR. Temperament, character, and personality disorders: Etiologic, diagnostic, treatment issues. Acta Psychiatr. Scand. 2002; 106: 189–195.

59. Miller JD, Campbell WK, Pilkonis PA, Morse JQ. Assessment procedures for narcissistic personality disorder: A comparison of the Personality Diagnostic Questionnaire-4 and best-estimate clinical judgments. Assessment 2008; 15: 483–492.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Correlation between the trait scales (22-item Tarumi’s Modern-Type Depression Trait Scale and Kasahara’s Inventory) and blood biomarkers among drug-free major depressive disorder (MDD) patients (N = 19).

Table S2. Comparison of blood biomarkers among 19 drug-free major depressive disorder (MDD) patients based on the cut-off score of 54 on TACS-22.

Table S3. The 22-item Tarumi’s Modern-Type Depression Trait Scale (TACS-22): Japanese version.