Title
The relationship between premorbid intelligence and symptoms of severe anorexia nervosa restricting type

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This thesis is based on the following published papers. Publications have be quoted and cited accordingly [1–3].

- Keizaburo Ogata, Ken Ichiro Koyama, Takamasa Fukumoto, Suguru Kawazu, Mihoko Kawamoto, Eriko Yamaguchi, Yuuki Fuku, Marie Amitani, Haruka Amitani, Ken Ichiro Sagiyama, Akio Inui, Akihiro Asakawa, "The relationship between premorbid intelligence and symptoms of severe anorexia nervosa restricting type," *Int J Med Sci.*, vol. 18, no. 7, pp. 1566–1569, 2021 [1].

- Keizaburo Ogata, Ken I Koyama, Marie Amitani, Haruka Amitani, Akihiro Asakawa, Akio Inui, "The effectiveness of cognitive behavioral therapy with mindfulness and an internet intervention for obesity: a case series," *Front Nutr.*, vol. 5, 56, pp. 1-5, 2018 [2].

- Keizaburo Ogata, Koji Ataka, Hajime Suzuki, Takakazu Yagi, Ayumi Okawa, Takamasa Fukumoto, Boyang Zhang, Masanori Nakata, Toshihiro Yada, Akihiro Asakawa, "Lavender oil reduces depressive mood in healthy individuals and enhances the activity of single oxytocin neurons of the hypothalamus isolated from mice: a preliminary study," *Evid Based Complement Alternat Med.*, vol. 2020, 5418586, pp. 1-9, 2020 [3].

Introduction

Rapid social change is thought to bring about a general increase in psychological pressure and stress [4]. The prevalence of psychiatric disorders is increasing, especially in developed countries, and is a social problem. The lifetime prevalence of any psychiatric disorder is estimated to be 20.3% in Japan [5], 13.2% in China [4], 27.6% in South Korea [6], and 34.2% in Saudi Arabia [7]. Furthermore, through a systematic review and meta-analysis, it was found that approximately one in five persons experienced a common psychiatric disorder within a 12-month period across 155 general population surveys undertaken in 59 countries [8].

Stress-related disorders include anorexia nervosa (AN), overweight, obesity, and mood disorders. AN is a psychiatric disorder which causes patients to pursue body weight loss [9, 10]. AN restricting type (AN-R) is characterized by severe emaciation with long-term food restriction, leading to behavior that contributes to the maintenance of low body weight [9]. Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a health risk. According to the global burden of disease, this issue has grown to epidemic proportions, with over 4 million people dying each year as a result of being overweight or obese in 2017 [11].

In recent years, the use of aromatherapy for therapeutic purposes has increased substantially; it is used to decrease pain, mental stress, and depression, and improve vital signs [12–15]. Aromatherapy is the use of pure essential oils from fragrant plants to help relieve health problems and improve quality of life in general [16]. In particular, the inhalation of lavender oil has attracted considerable attention in aromatherapy, as a method for reducing stress without medication [17, 18].

This study consists of three component studies: the main study and two pilot studies. The first study examines the relationship between AN-R symptoms and scores of neuropsychological and psychological tests in patients with severe AN-R [1]. The second study investigates the effectiveness of cognitive behavioral therapy with mindfulness and internet interventions for overweight individuals [2]. The third study examines the effects of short-term exposure to lavender oil on autonomic nervous system parameters and psychological tendencies in healthy adult men [3].

Study 1

The relationship between premorbid intelligence and symptoms of severe anorexia nervosa restricting type

Abstract

The purposes of this study were as follows: to compare premorbid IQ with present IQ in patients with more severe anorexia nervosa restricting type (AN-R) and to investigate the relationship between decreasing IQ and symptoms in patients with severe AN-R.

Twenty-two participants were recruited (12 were AN-R patients; 10 were healthy controls). The average body mass index (BMI) in AN-R patients and healthy controls was 12.65 and 19.82, respectively. We assessed the outcomes using the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III), the Japanese Adult Reading Test, the Eating Disorders Inventory-2 (EDI-2), the Beck Depression Inventory-2 (BDI-2), the State-Trait Anxiety Index (STAI), and the Wechsler Memory Scale-Revised (WMS-R).

In two-way repeated ANOVA, there were significant interactions for the full-scale IQ (FIQ) and performance IQ (PIQ). Only in the AN-R group, a significant single main effect of time was evidenced for the FIQ and PIQ. In the AN-R group, a significantly high positive correlation was found between changes in the PIQ and the body dissatisfaction subscale of the EDI-2. In the WMS-R study, although there was a significant difference in the education years between control and AN-R, delayed recall of AN-R is aligned with the lower limit of the normal range.

These findings raise the possibility that in patients with severe AN-R, an excessive decrease in body weight induces decreased PIQ; as a result, they have worse dissatisfaction with their body shape.

1.1. Background

Anorexia nervosa (AN) is a psychiatric disorder that pursue body weight loss [9, 10]. AN restricting type (AN-R) is characterized by severe emaciation with long-term food restriction, leading to behavior that contributes to the maintenance of a low body weight [9]. Some studies have reported that the age-adjusted and gender-adjusted incidence of AN is approximately 4.7 per 100,000 persons (95% Cl: 3.6-5.8) in the UK [19] and 8.3 per 100,000 persons (95% Cl: 7.1-9.4) in the USA [20]. The age-adjusted incidence rate of AN showed a significant increasing trend only in females in late puberty-early adolescence [20, 21]. The mortality rate of AN is 5.1 deaths (95% Cl: 3.99-6.14) per 1,000 person-years; one in five individuals with AN who died had committed suicide [22].

Cognitive behavioral therapy (CBT) [23, 24], “the third wave” CBT [25], and family therapy [26, 27] are reported as treatment approaches for AN. However, no clear primacy of one approach has been identified for AN [28]. Treatment for AN is often arduous because its pathogenesis is not entirely understood. One important problem of AN is partial cognitive deficit. We reported in a previous study that patients with AN have a low intelligence quotient (IQ) [29]. However, some studies have reported that patients with AN have an average IQ [30–32]. What accounts for the difference in the results between these studies? One of the apparent differences is the patient’s body mass index (BMI). We have reported a low IQ among AN patients with very low BMI (average 12.8) compared to that of patients in other reports (average BMI; 15.4-18.3) [29]. These findings indicate that lower BMI with AN may decrease the patient’s IQ. Therefore, the question of whether decreasing IQ in patients with AN with low BMI is the cause or effect is thought to be very important.

The National Adult Reading Test (NART) is a word-reading test (50 short words of irregular pronunciation) widely used in research and clinical practice as an estimate of premorbid intellectual ability [33]. It has high construct validity as a measure of general intelligence and high levels of interrater and test-retest reliability. There are strong correlations between the NART and the Wechsler Adult Intelligence Scales (WAIS) performance IQ (PIQ) (r = .724) [34]. Some studies have reported that patients with AN have a normal IQ as measured by the NART [35]. However, there are no reports that compare the NART and the WAIS in the same patients with AN. Concerning memory performance, there is ample evidence to suggest that eating disorder-related information is selectively processed by AN patients, resulting in enhanced memory function for AN-related stimuli in incidental, explicit, and self-referential memory tasks (“memory bias”) [36, 37]. However, in previous studies, assessments of AN patients were done using only part of the Wechsler Memory Scale-Revised (WMS-R), that is only a neuropsychological assessment of memory intelligence quotient was done [38], and it is difficult to say whether memory intelligence quotient was accurately and comprehensively assessed.

The purposes of this study were as follows: to compare premorbid IQ with present IQ in patients with more severe AN-R and to investigate the relationship between decreasing IQ and symptoms in patients with severe AN-R.

1.2. Materials and methods

1.2.1. Participants

The patients were consulted for medical treatment at Kagoshima University Hospital. Volunteers were recruited by a notice board that was placed on Kagoshima University.

All participants met with researchers, the study plan was explained in detail, and all participants signed informed consent forms. The inclusion criteria for patients were as follows: (1) patients met the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition TR criteria for AN-R, (2) their body mass index (weight in kg/height in m^2; BMI) was 15 or less, and (3) an examination was feasible. The exclusion criteria for patients were as follows: (1) had comorbidities, and (2) were less than 18 years old.

1.2.2. Outcome measurement

Cognitive function assessments

The Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) and the Japanese Adult Reading Test (JART) were used.

The WAIS-III is a neuropsychological assessment of intelligent quotient that provides four indices, each based on a different set of subtests (full-scale IQ (FIQ), verbal IQ (VIQ), performance IQ (PIQ), verbal comprehension (VC), perceptual organization (PO), working memory (WM), and processing speed (PS)), making it a more comprehensive conception of cognitive function [39]. In this study, FIQ, VIQ, PIQ, VC, PO, WM, and PS were used.

The JART is the Japanese version of the National Adult Reading Test (NART) [40]. The NART provides estimates of premorbid intelligence through the use of reading tasks with 50 English words. On the JART, the task was changed to Japanese Kanji words. This assessment can speculate on the premorbid IQ of dementia patients by the number of correct answers for 50 Japanese kanji idioms (e.g., “不如帰”, “自惚”).

The WMS-R is a neuropsychological assessment of memory intelligence quotients [41], each based on a different set of subtests: memory IQ (MIQ), verbal MIQ (Verbal MIQ), visual MIQ (Visual MIQ), attention/concentration (AC), delayed recall (DC). In this study, MIQ, Verbal MIQ, Visual MIQ, AC, and DC were used.

Psychological tests

The Eating Disorders Inventory-2 (EDI-2), the Beck Depression Inventory-2 (BDI-2) and the State-Trait Anxiety Index (STAI) were used.

The EDI-2 is a 91-item self-report inventory instrument for assessing symptoms and psychosocial factors associated with eating disorders and includes 11 subscales (drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interceptive awareness, maturity fears, asceticism, impulse regulation, social insecurity). Items are rated on a 6-point scale, with responses ranging from never to

always. In accordance with EDI-2 scoring procedures, item scores were recorded on a 4-point scale (0 to 3) to form subscale scores [42].

The BDI-2 is a 21-item self-report inventory that measures depressive symptoms such as sadness, pessimism, suicidal thoughts or wishes, tiredness or fatigue, loss of energy, and loss of pleasure, among other [43, 44]. Each item is scored on a scale from 0 to 3, with a higher score indicating more serious depressive symptoms and total scores ranging from 0 to 63.

The STAI is a 40-item self-report instrument that is widely used and extensively researched in the assessment of state and trait anxiety [45, 46]. State anxiety is regarded as having a transitory nature and is characterized by subjective feelings such as tension, apprehension and nervousness. Trait anxiety refers to relatively stable individual differences in anxiety proneness. Each item is rated on a 4-point Likert scale ranging from 1 to 4, with a higher score indicating more serious anxiety symptoms and total scores ranging from 20 to 80.

1.2.3. Statistical analysis

SPSS Statistics 22 was used for statistical analysis. Comparisons of averages between groups (AN-R and control) were based on Student's t-test and two-way repeated measures analysis of variance (ANOVA). Associations between IQ changes due to weight loss and psychological tests (EDI-2, BDI-2 and STAI) were estimated with correlation coefficients in the AN-R group.

1.2.4. Ethical considerations

This study was approved by the Clinical Research Ethics Committee of Kagoshima University (registered No. 25-018). Written informed consent was obtained from all participants before participation.

1.3. Results

Twenty-two participants were recruited (12 were AN-R patients; 10 were healthy controls), out of which 17 (nine were AN-R patients; eight were healthy controls) were assessed using WMS-R. The participants were women, had a history of disease for more than one year, and had received different individualized treatment protocols. Table 1 shows the characteristics of the participants. The average BMI in AN-R patients and healthy controls was 12.65 and 19.82, respectively. There were significant differences in BMI and scores on the WAIS (FIQ, VIQ, PIQ and PO), JART (premorbid FIQ, premorbid VIQ and premorbid PIQ), EDI-2, BDI-2 and STAI (Table 1). In two-way repeated

measures ANOVA, there were significant interactions for the FIQ ($F (1, 20) = 6.06$, $p < .05$) and PIQ ($F (1, 20) = 21.78$, $p < .01$) (Table 2). Only in the AN-R group, a significant single main effect of time was evidenced for the FIQ ($F (1, 20) = 20.77$, $p < .01$) and PIQ ($F (1, 20) = 41.21$, $p < .01$). In the AN-R group, a significantly high positive correlation was found between changes in the PIQ and the body dissatisfaction subscale of the EDI-2 (Table 3). In the memory study, there were significant differences in education years and the WMS-R score (MIQ, Visual MIQ, AC, and DR) (Table 4).

1.4. Discussion

This is the first study to compare premorbid IQ with present IQ in patients with more severe AN-R and conduct multiple investigations of the relationship between decreasing IQ and symptoms in severe AN-R using psychological tests. Previous studies in AN patients (average BMI 15.4-18.3) reported normal IQ using the WAIS-R or the WAIS-III [31–33]. However, in the present study, the full IQ and cognitive functioning (particularly PO) scores in patients with AN-R indicated almost borderline IQ. The difference between the results of the previous study and those of the present study was thought to be due to the difference in the BMI scores of the study participants. Furthermore, a previous study that administered the WAIS-III among patients with severe AN-R reported results that were similar to those of this study [29]. In addition, previous studies have reported that IQ scores (FIQ, PIQ, and PO) recover significantly with weight re-gain [29]. It is speculated that weight re-gain through CBT and nutritional treatment will restore the reduced IQ in patients with severe AN.

In this study, the JART showed significant differences when the premorbid FIQ, premorbid VIQ and premorbid PIQ in AN-R patients were compared with those in healthy controls. However, considering that the IQ score is defined as mean = 100 and SD = 15, the results of premorbid IQ in AN-R were normal [39]. Therefore, these findings indicate that premorbid IQ might not be a risk factor for severe AN-R, although the number of patients in this study was limited. Future studies that include larger samples could address this limitation.

AN-R patients are dissatisfied with their figures and lose body weight [47, 48]. They decrease their food intake and over-exercise, even though they are facing a life crisis. In this study, there were no correlations between a drive for thinness and decreased IQ. This result was similar to that of a previous study [29]. However, in the AN-R group, a strong positive correlation was found between the decreased PIQ and the body dissatisfaction subscale of the EDI-2 (Table 3). A person with a low PIQ has a slow information processing speed [39]. It is difficult for the person to develop a greater understanding of

larger concepts and grasp abstract content. In addition, people with low PIQ have low visual-spatial cognitive ability and difficulty doing multiple things at the same time. These findings raise the possibility that in patients with severe AN-R, an excessive decrease in body weight induces decreased PIQ; as a result, they have worse dissatisfaction with their body shape.

Although there was a significant difference in the education years between control and AN-R in the WMS-R, there were significant differences in MIQ, Visual MIQ, AC, and DR. However, considering that the IQ score is defined as mean = 100 and SD = 15, the results of MIQ, Visual MIQ, AC, and DR in AN-R are normal [41]. DR of AN-R is aligned with the lower limit of the normal range (DR = 85.89). Therefore, possibly, long-term memory of severe AN-R is impaired, but further investigation, including increasing the number of participants, will be necessary.

We have revealed that patients with severe AN-R have normal premorbid IQ and decreased postmorbid IQ; furthermore, their postmorbid PIQ is remarkably low. Therefore, given this decreased IQ, including PIQ, we should treat severe AN-R patients.

Study 2

The effectiveness of cognitive behavioral therapy with mindfulness and an internet intervention on overweight: a case series

Abstract

It is difficult for obese (body mass index of more than 30) and overweight (body mass index of 25-30) people to reduce and maintain their weight. The aim of this case series was to examine the effectiveness of a new cognitive behavioral therapy (CBT) program that combines mindfulness exercises (e.g., the raisin exercise and breathing exercises) and an online intervention to prevent dropout and subsequent weight gain in overweight participants. This case series included three participants, for whom previous weight reduction programs had been unsuccessful. All participants completed the program (60-min, group sessions provided weekly for 9 weeks) and an 18-month follow-up assessment. Results showed that all participants succeeded in losing weight (loss ranged from 5.30 to 8.88% of their total body weight). Although rebound weight gain is commonly observed in the first year following initial weight loss, the follow-up assessment showed that participants achieved further weight loss during the 18-month follow-up period. These results suggest that a CBT program that comprises mindfulness and an online intervention may be an effective method for weight loss and maintenance, and may prevent dropout in obese and overweight individuals.

2.1. Background

The basic strategies involved in the treatment of obesity (body mass index; BMI over 30) and overweight (BMI between 25 and 30) include lifestyle improvements, exercise therapy, and cognitive behavioral therapy (CBT). The structure of standard CBT for obesity and overweight includes self-monitoring, goal-setting, stimulus control, behavioral substitution, and cognitive restructuring [49]. Numerous studies have reported that the use of CBT is successful in reducing patients' weight during treatment. However, many patients subsequently regain weight and fail to maintain weight reduction following the completion of treatment [50]. In addition, the results of a randomized controlled trial by Cooper et al. found that a new treatment program aimed at weight maintenance was no more effective, relative to basic treatment, in preventing patients from regaining weight [51]. These findings indicate that treatment for obesity should be extended to maintain patients' weight loss. Moreover, patients frequently drop out of obesity treatment programs, which further complicates the success of treatment [52, 53]. Although increasing the frequency of the interventions could prevent dropout and

maintain patients' motivation, it could also lead to several problems involving health resources by increasing patients' physical, temporal, and psychological burden, which could result in further dropout. Therefore, interventions that are implemented frequently and that reduce these types of burden are required. In this regard, the provision of CBT via the Internet (iCBT) has recently been shown to be as effective as face-to-face treatment for conditions such as depression, anxiety, and insomnia [54–56]. Moreover, therapist-guided iCBT may be less time consuming, relative to face-to-face treatment, for both individual and group therapy [57]. In addition, mindfulness, which is one of the main concepts in third-wave CBT, is well known for its effectiveness in the treatment of anxiety, depression, and impulsive eating [58–60]. Given the promise of both iCBT and mindfulness interventions, we developed a new program involving mindfulness exercises and an online intervention for obesity to prevent participant dropout and improve psychological health. The purpose of this case series was to determine the effectiveness of Cognitive Behavioral Therapy with Mindfulness exercise and an Internet intervention for Obesity (CBT-MIO).

2.2. Method

2.2.1. Participants

Participants were recruited via an advertisement placed on the notice board at Kagoshima University in December 2014. The inclusion criteria were as follows: (a) between 18 and 60 years of age, (b) BMI (weight in kg/height in m^2) between 25.0 and 40.0, (c) previous lack of success in weight reduction programs, (d) availability to participate in treatment for 9 weeks, (e) access to the Internet on a daily basis, and (f) willingness to participate in the study. The exclusion criteria were as follows: (a) consultation with a doctor for type 1 or 2 diabetes, cardiovascular disease, or mental health disorders, (b) pregnancy, and (c) weight loss within the preceding 6 months because of weight loss success. Table 5 shows the characteristics of participants. Three participants (two female) were included in the study. The age of participants was in 20–30 years, and they were defined as overweight. One of trait anxiety was high (Participant B) however state anxiety of all participants was in the normal range [45, 46]. All participants attended a follow-up assessment 18 months after the final weight loss session.

2.2.2. CBT-MIO

CBT-MIO was developed based on a well-known CBT program for weight loss and maintenance [50, 51]. CBT-MIO aims to aid participants in losing between 5% to 10% of their total body weight and consists of four elements: (a) a psychoeducational intervention

designed to promote a healthy diet and physical exercise, and to reduce self-sabotaging thoughts; (b) self-monitoring of daily food-intake using a notebook and the use of a social networking sites (SNSs) to upload photographs of self-reported food consumption during the final 4 weeks of the program; (c) mindfulness exercises (e.g., raisin exercise and mindful breathing [61]) to increase distress tolerance, improve healthy coping strategies, and reduce maladaptive coping strategies (e.g., avoidant and impulsive coping styles that involve emotional eating); and (d) relearning adaptive eating habits. The diet program consisted of weekly 60-min group sessions implemented for 9 weeks. The program was divided into two sections. Specifically, during the first 4 weeks of the program, participants received only face-to-face therapy, and in the subsequent 5 weeks of the program, participants were required to upload their daily food intake and activities to an SNS page (e.g., Facebook) and discuss them with other participants in a supportive manner (Figure 1). Participants and therapists made positive comments regarding participants' adaptive eating behaviors and suggested additional ideas concerning adaptive thoughts and the implementation of action plans in critical situations involving food-related temptation, such as dinner parties. A follow-up assessment was performed 18 months later.

2.2.3. Outcomes

The primary outcome was BMI, which was calculated using participants' weight and height, and secondary outcomes were scores on the Dutch Eating Behavior Questionnaire (DEBQ) [62, 63], the State-Trait Anxiety Inventory (STAI) [45, 46], and the Five Facet Mindfulness Questionnaire (FFMQ) [64, 65]. The DEBQ is a 33-item self-report questionnaire that assesses comprehensive eating behavior associated with obesity. It contains subscales for three different types of eating behaviors: restrained, emotional, and external eating. Total scores on each subscale are derived from average item responses, with higher scores reflecting greater emotional and external eating, and lower scores reflecting more restrained eating. The STAI is a 40-item self-report instrument that is widely used for the assessment of state and trait anxiety. State anxiety is transitory in nature and is characterized by subjective feelings of tension, apprehension, and nervousness. Trait anxiety refers to relatively stable individual differences in anxiety proneness, with higher scores indicating more serious symptoms of anxiety. The FFMQ is a 39-item self-report questionnaire that measures five aspects of mindfulness: observing, describing, acting with awareness, nonjudging, and nonreactivity to inner experience. Observing means noticing or attending to internal and external experiences, such as sensations, thoughts, or emotions. Describing refers to labeling internal

experiences with words. Acting with awareness includes focusing on one's activities in the moment as opposed to behaving mechanically. Nonjudging refers to taking a non-evaluative stance toward thoughts and feelings. Nonreactivity to inner experience refers to allowing thoughts and feelings to come and go, without being caught up in or carried away by them. Each item is rated on a 5-point Likert scale (1 = Never or rarely true; 5 = Very often or always true), with higher scores reflecting greater mindfulness. BMI was assessed at every session, and the DEBQ, the STAI, and the FFMQ were administered at baseline (Session 1), Session 9, and the follow-up assessment 18 months after Session 9.

2.3. Ethics

The study was approved by the University of Kagoshima Human Research Ethics Committee (registered No. 26-13). Written informed consent was obtained from all participants before participation.

2.4. Result

Figure 2 shows the participants flow through this case series. All participants succeeded in losing more than 5% of their total body weight. The proportions of total body weight lost by individual participants were 6.91% (Participant A), 5.30% (Participant B), and 8.88% (Participant C). As shown in Table 5, all participants also exhibited additional weight loss at the follow-up assessment (Participant A: 13.98%, Participant B: 7.91%, Participant C: 10.98%). Moreover, relative to baseline, participants' scores on the DEBQ restrained subscale and the FFMQ increased, whereas their scores on the DEBQ emotional and external subscales and the STAI decreased (Table 6).

2.5. Discussion

The purpose of this case series was to examine the effectiveness of CBT-MIO in previously unsuccessful overweight participants, which was designed to promote weight loss and prevent dropout and subsequent weight gain. With respect to dropout, all of the participants completed the program, including the follow-up assessment, suggesting that CBT-MIO was effective in preventing dropout. With regard to weight reduction, all participants succeeded in losing more than 5% of their total body weight. Considering that the weight loss goals for obese and overweight individuals in previous studies using CBT are between 5 and 10% [50, 51, 66, 67], the rate of weight reduction in the current study was satisfactory. In addition, while rebound weight gain is commonly observed in the first year following initial weight loss, all of the participants in the current study achieved further weight loss during the 18-month follow-up period [68]. Furthermore, all

of the participants demonstrated positive changes in psychological health, and these effects persisted at the 18-month follow-up assessment. These positive changes in psychological health may have resulted from the mindfulness exercise, as previous research has also found that mindfulness interventions reduce the STAI scores and increase the FFMQ scores [69, 70]. In view of these findings, the mindfulness exercises designed to promote appropriate eating behavior in CBT-MIO were effective in improving participants' psychological health, as reflected by changes in their DEBQ, STAI, and FFMQ scores. These results indicate that simply noticing bodily sensations, thoughts, memories, emotions, and fantasies via mindfulness exercises may be a particularly salient feature in changing conditioned patterns of eating [71]. Indeed, during CBT-MIO sessions in the current study, participants reported that they recognized their impulse to eat and their automatic eating behaviors (e.g., binge eating, picking, and stress-related eating) by achieving a "here and now" awareness of their behavior, thoughts, bodily sensations, and feelings. In doing so, they were able to consider alternative cognitive behavioral plans for eating. Therefore, mindfulness may serve as a reminder that prompts individuals to use established cognitive behavioral strategies in managing their eating behaviors, instead of reverting to more maladaptive coping strategies. Despite the above findings, the current study is subject to several limitations. First, the study sample was very small. In addition, the study was a single-arm, open study that did not include a control group. Moreover, participants used their smartphones to upload photographs of self-reported food consumption onto SNSs. Given that all participants in the current study were familiar with smartphones, this program would not be suitable for individuals who do not use or are not familiar with smartphones (e.g., older adults or individuals with financial problems). Future studies that include larger samples and control groups, such as randomized controlled trials, could address these limitations.

Study 3

Lavender oil reduces depressive mood in healthy individuals: a pilot study

Abstract

The aim of the present study was to assess the effects of lavender oil inhalation on blood pressure, pulse measurements, cortisol levels, depressive mood, and anxiety in healthy male adults. The participants (n = 7) were aged 20 - 40 years. After randomization, they received an inhaled dose of lavender oil or distilled water for 20 min. They received the other treatment after a washout period of one week. We assessed the outcomes using the Self-Rating Depression Scale (SDS), State-Trait Anxiety Inventory (STAI), and self-rated unidimensional Visual Analogue Scale for depression; anxiety; and hunger, thirst, and appetite, respectively. Blood pressure, pulse rate, and cortisol concentration in the peripheral blood were assessed before and after inhalation. Seven participants completed the study. Lavender inhalation decreased SDS Scale score and systolic and diastolic blood pressure. Lavender oil might be useful for stress relief.

3.1. Background

Lavandula angustifolia (lavender) essential oil is approved as a herbal medicine by the European Medicine Agency and has been used as a therapeutic and cosmetic agent for centuries. Lavender oil reportedly has sedative, relaxing, and anti-infectious effects and has been shown to improve sleep quality [72, 73]. Inhalation of lavender oil has lately attracted considerable attention in aromatherapy, which is a method for reducing stress without medication. Lavender aromatherapy has been reported to decrease autonomic parameters, such as blood pressure and heart rate [13]. Lavender oil inhalation has also been reported to decrease postpartum depression [14, 15] and the anxiety levels during gynaecological examination [74]. However, several limitations are associated with these prior studies, such as the lack of a control group, and the mixing of lavender with other oils was used in the studies [14, 15]. Even where a control group was present, no vehicle was used [14, 15, 74]. The aims of this study were to assess the effects of lavender on autonomic parameters such as blood pressure and pulse rate, mood such as depressive mood and anxiety, and appetite scores in healthy volunteers.

3.2. Methods

3.2.1. Participants

Nine participants were included in the study. the inclusion criteria were as follows: subjects (1) male; (2) age: 40 $\geqq$ aged $\geqq$ 20 years; (3) with no serious anamnestic

history (cardiovascular disease, respiratory disease, or mental health disorders); (4) healthy; (5) no experience with aromatherapy; and (6) able to participate in this experiment at the same time every other week. the exclusion criteria were as follows: subjects (1) female; (2) age: aged < 20 years or > 40 years; and (3) a serious anamnestic history (cardiovascular disease, respiratory disease, or mental health disorders). A written informed consent, indicating that the participants were able to withdraw from the study at any point if they did not agree with the study, was obtained from all the participants.

3.2.2. Study design

A pilot study was conducted from January to February 2017. This study involved two inhalation treatments: lavender oil and distilled water (vehicle). Distilled water was chosen because it has no fragrance. A lavender-vehicle/vehicle-lavender design was adopted. Block randomization was selected because of the small number of participants [75]. In this pilot study, a fictitious subject was chosen via a randomization procedure because the number of subjects enrolled in the experiment was an odd number. Assignments were randomly determined by an independent dentist in a 1 : 1 ratio in blocks. Random numbers were provided using Microsoft Excel (version 2013; Microsoft, Redmond, WA, USA). The experimental condition was written on paper in nontransparent envelopes, and the experimenter was allowed to know the experimental conditions by opening the envelope.

3.2.3. Interventions

Lavender oil derived from the Lavandula angustifolia flower was purchased from Pranarom Co., Ltd. (Ghislenghien, Belgium). All experiments were conducted at the Kagoshima University hospital in the morning at the same time. The participants were required not to eat after 8 p.m. on the day before the examination until the end of the examination. Before starting the experiment, the participants responded to questions regarding the previous use of lavender, anamnestic history, experiment day's medical condition, and whether or not the participants were fasting. the participants underwent blood drawings, blood pressure measurements, pulse measurements, and psychological assessments. Following this, for the purpose of keeping the inhalation concentration of lavender oil constant among the participants, 75 μl (1 drop) of lavender oil or distilled water was dropped from a height of less than 30 cm from the lower jaw using a micropipette (PIPETMAN P200; GILSON Inc., Middleton, WI, USA) on the dental apron placed on the participants, and they were exposed to the scent of lavender oil or distilled water through nasal or oral breathing for 20 min. After this, the participants once again

underwent blood drawings, blood pressure measurements, pulse measurements, and psychological tests. Both treatment sessions were separated by a one-week washout period.

3.2.4. Outcome measurement

The Self-Rating Depression Scale (SDS), the State-Trait Anxiety Inventory (STAI), and self-rated unidimensional Visual Analogue Scale (VAS) were used to assess depressive mood; anxiety; and hunger, thirst, and appetite, respectively. The SDS is a widely used and an extensively researched questionnaire for the evaluation of the degree of depression [76]. In this case, we used the Japanese version of this questionnaire [77]. The SDS consists of 20 items, rated on a 4-point Likert scale with total scores ranging from 20 to 80. The STAI is the most commonly used self-reported state (actual, STAI-S) and trait (stable, STAI-T) anxiety scale [78]. The STAI consists of 20 items each related to state and trait, rated on a 4-point Likert scale with total scores ranging from 20 to 80. In this case, we used the Japanese version of the questionnaire [46]. In this pilot study, state anxiety was determined before and after exposure. VAS was used to evaluate the perception of hunger, thirst, and appetite. Subjects were requested to make a vertical mark on each of a 100 mm horizontal line oriented from left to right (e.g., “hungry” and “not hungry”) that best matched how they were feeling at the time. To evaluate each of the sensations, each score was determined by measuring the distance from the left side of the line to the mark.

3.2.5. Cortisol concentration in the peripheral blood

Blood sampling was conducted before and after exposure by a nurse, and the samples were collected using a sterilized microtube. We requested the Clinical Pathology Laboratory Co., Ltd. (Kagoshima, Japan) to measure the concentrations of cortisol (using a chemiluminescent immunoassay method).

3.2.6. Statistical analysis

SPSS Statistics 22 was used for statistical analysis. Differences among groups (lavender/control) and time (before/after) in SDS, STAI, VAS, blood pressure, pulse rate, and cortisol concentration in the peripheral blood were determined by two-way analysis of variance (ANOVA); multiple comparisons were tested using the Bonferroni method.

3.2.7. Ethical considerations

The clinical study was approved by the Clinical Research Ethics Committee of

Kagoshima University (26-154).

3.3. Results

3.3.1. General Characteristics of the Participants

Nine persons were assessed for eligibility, while two persons were excluded in this study because one felt unwell and the other decided not to participate. Seven participants out of 9 subjects met the eligibility criteria (Figure 3). One subject was unwell on the day of the experiment, and another subject was absent for personal reasons. All participants were healthy males, with a mean age of 28.0 (range 23-33-year-old). The body mass index (BMI) was 22.58 ± 0.87 kg/m^2.

3.3.2. Blood Pressure

In systolic blood pressure, there was significant interaction ($F(1, 12) = 15.41$, $p < .01$, Table 7, Figure 4). In the lavender group, the post-systolic blood pressure was lower than the presystolic blood pressure and the control post-systolic blood pressure. In diastolic blood pressure, there was significant interaction ($F(1, 12) = 5.83$, $p < .05$, Table 7, Figure 4). In the lavender group, the post-diastolic blood pressure was lower than the pre-diastolic blood pressure. In pulse rate, the effect of time was observed between before and after ($F(1, 12) = 8.52$, $p < .05$, Table 7, Figure 4).

3.3.3. Questionnaires: SDS, STAI, VAS

In the SDS, there was significant interaction ($F(1, 12) = 7.85$, $p < .05$, Table 7, Figure 4). The post-SDS was lower than the pre-SDS. In the STAI-S, the effect of time was observed between pre-exposure and post-exposure ($F(1, 12) = 13.90$, $p < .05$, Table 7, Figure 4). In VAS, there was no significant difference between the lavender and the vehicle group (Table 7, Figure 4). All participants showed no changes in the STAI-T score between pre-exposure and post-exposure (Table 7, Figure 4).

3.3.4. Cortisol

The pre-cortisol levels (μg/dl) were 15.51 ± 1.12 in the vehicle and 14.94 ± 0.96 in the lavender inhalation group, and the post-cortisol levels were 13.53 ± 1.54 in the vehicle and 12.77 ± 1.46 in the lavender inhalation group (Table 7, Figure 4). The effect of time was observed between pre-inhalation and post-inhalation ($F(1, 12) = 10.57$, $p < .01$); however, there was no significant difference between the lavender and the vehicle group (Table 7, Figure 4).

3.4. Discussion

Inhalation of lavender essential oils reduced the systolic and diastolic pressures and the SDS scores in this pilot study. The results of the present study suggest that the reduction of depressive mood and blood pressure may be achieved upon short-term exposure to lavender due to its relaxing effects. The usefulness of aromatic essential oils for inhalation in waiting rooms of mental health treatment [79] and hand massage therapy centers [80] has been reported. Aromatherapy using lavender essential oils has been applied for the treatment of various disorders and is supported by scientific evidence. The favorable effect of lavender on mood is an expected outcome of lavender intervention. Lavender has been reported to reduce depression and improve the quality of sleep and pain [72, 81]. Recently, Hassanzadeh et al. reported that aromatherapy with lavender essential oils decreased the levels of fatigue in patients undergoing haemodialysis compared to the Benson relaxation techniques [82]. Furthermore, S´anchez-Vidaña et al. indicated that inhalation of lavender essential oils ameliorates depression-like behaviour and increases neurogenesis in rats [83]. These relaxation effects of lavender are thought to arise from not only psychological effects but also physiological effects of the volatile components [84]. Lavender oil includes linalool and linalyl acetate as main components [85, 86]. Linalool from aromatic plants is under consideration as a medical ingredient. Linalool has been reported to possess various bioactivities: anti-inflammatory, anticancer, antihyperlipidaemic, antimicrobial, antinoceptive, analgesic, neuroprotective, and antidepressive properties [87]. Linalool was reported to reduce blood pressure and has been suggested to have direct effects on vascular smooth muscle leading to vasodilation in the rabbit carotid artery [88]. In addition, linalool has been demonstrated to be an antidepressant in mice [89]. Linalyl acetate has been reported to have antihypertensive properties in a hypertension-related ischemic injury model in rodents [90] and has also been shown to induce the recovery of the acute nicotine-induced cardiovascular disruptions in rodents [91]. However, there is a lack of literature mentioning the influences of linalool, linalyl acetate, and lavender on central neurons. Lavender oil is sensed by the olfactory epithelium, which sends signals through the limbic system to the hypothalamic tuberomammillary nucleus. This signal is then sent to the hypothalamic suprachiasmatic nucleus. Finally, this information elicits changes in autonomic nerve activity [85]. Wang et al. demonstrated that inhalation of 10% lavender activated the primary olfactory cortex, entorhinal cortex, hippocampus and parahippocampal cortex, thalamus, hypothalamus, orbitofrontal cortex, and insular cortex and its extension into the inferior lateral frontal region in healthy participants using functional magnetic resonance imaging (fMRI) [92]. These results suggest that the scent of lavender may influence the

functions of central nervous system.

3.5. Limitation

This study had some limitations. One of the most consistent biological findings in severe depression is the increased amount of plasma cortisol [93, 94]. In this study, there was no difference in cortisol levels between the lavender and vehicle groups, but there were differences in terms of depressed mood and blood pressure. Future studies should include participants who are experimentally stressed prior to lavender exposure, or the experimental condition should involve long-term rather than short-term exposure.

Conclusion

The results of Study 1 suggest that dissatisfaction with body shape in severe AN-R cases is influenced by extreme thinness. Therefore, interventions for body shape dissatisfaction may be useful after patients regain their weight. Moreover, it would be useful to conduct longitudinal IQ tests using the WAIS as a treatment outcome for severe AN-R. In Study 2, all participants succeeded in losing weight and the follow-up assessment showed that participants achieved further weight loss during the follow-up period. These results suggest that CBT-MIO may be an effective method to facilitate weight reduction in overweight individuals, not only by promoting weight loss but also by preventing patient-dropout and subsequent weight gain. In Study 3, the inhalation of lavender oil was found to be effective in decreasing the SDS score and systolic and diastolic blood pressure, indicating that lavender oil might be useful for stress relief.

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Table 1. Clinical characteristics of the participants

	Control		AN-R		t	p	Cl
	Mean	SD	Mean	SD			
Age	32.40	9.65	32.17	14.45	-0.05	0.964	-11.05, 10.58
Education years	14.00	1.41	12.75	2.22	-1.60	0.126	-2.89, .39
BMI (kg / m^2)	19.82	1.81	12.65	1.47	-10.26*	0.000	-8.62, -5.71
WAIS-III							
FIQ	103.20	10.26	81.00	13.37	-4.30*	0.000	-32.98, -5.71
VIQ	101.40	12.74	85.42	14.13	-2.76**	0.012	-28.06, -3.91
PIQ	103.50	8.55	78.92	10.72	-5.86*	0.000	-33.34, -15.83
VC	97.70	10.76	89.67	13.18	-1.54	0.138	-18.89, 2.82
PO	100.00	6.52	76.08	10.36	-6.32*	0.000	-31.81, -16.02
WM	100.00	14.16	87.58	14.51	-2.02†	0.057	-25.24, .40
PS	106.10	16.11	92.17	22.17	-1.65	0.114	-31.51, 3.64
JART							
premorbid FIQ	106.30	3.95	96.58	6.75	-4.20*	0.001	-14.57, -4.86
premorbid VIQ	108.60	4.65	96.67	7.55	-4.35*	0.000	-17.66, -6.21
premorbid PIQ	102.10	2.96	96.83	4.82	-3.01*	0.007	-8.92, -1.61
EDI-2	31.20	26.57	81.42	39.20	3.44*	0.003	19.76, 80.67
BDI-2	6.00	4.14	20.92	12.07	4.01*	0.001	6.93, 22.90
STAI-State	42.00	8.56	53.17	12.86	2.34**	0.030	1.23, 21.11
STAI-Trait	38.30	5.23	52.67	10.82	4.06*	0.001	6.89, 21.84

$^{\dagger}p < .10$, $^{*}p < .05$, $^{**}p < .01$

Control = 10, AN-R = 12; AN-R, anorexia nervosa restricting type; BMI, body mass index; WAIS-III, Wechsler adult intelligence scale third edition; FIQ, full-scale intelligence quotient; VIQ, verbal intelligence quotient; PIQ, performance intelligence quotient; VC, verbal comprehension; PO, perceptual organization; WM, working memory; PS, processing speed; JART, Japanese adult reading test; EDI-2, eating disorders inventory-2; BDI-2, beck depression inventory-2; STAI, state trait anxiety inventory; Results are expressed as mean ± SD; Cl, 95% confidence interval

Table 2. Two-way repeated measures ANOVA (group × time) results

		Time		F-number		
		Pre	Post	Group	Time	Interaction
FIQ	Control	106.30 ± 3.95	103.20 ± 10.26	25.82**	13.57**	6.06*
	AN-R	96.58 ± 6.75	81.00 ± 13.37			
VIQ	Control	108.60 ± 4.65	101.40 ± 12.74	16.01**	10.20**	0.49
	AN-R	96.67 ± 7.55	85.42 ± 14.13			
PIQ	Control	102.10 ± 2.96	103.50 ± 8.55	36.78**	15.92**	21.78**
	AN-R	96.83 ± 4.82	78.92 ± 10.72			

†p < .10, *p < .05, **p < .01

AN-R, anorexia nervosa restricting type; FIQ, full-scale intelligence quotient; VIQ, verbal intelligence quotient; PIQ, performance intelligence quotient

Table 3. The correlation between IQ changes and psychological scale with weight loss

	FIQ	VIQ	PIQ
Age	.35	.41	.23
BMI	.13	.06	.26
EDI-2	.26	.24	.26
drive for thinness	.22	.17	.23
bulimia	.21	.21	.16
body dissatisfaction	.49	.42	.60*
ineffectiveness	.21	.25	.09
perfectionism	.45	.44	.46
interpersonal distrust	.17	.16	.16
interceptive awareness	-.06	-.09	-.06
maturity fears	.08	.07	.10
asceticism	.17	.16	.20
impulse regulation	.14	.14	.13
social insecurity	.01	.03	-.02
BDI-2	.01	.02	-.04
STAI-State	.20	.18	.19
STAI-Trait	.17	.17	.14

*$p < .05$

FIQ, full-scale intelligence quotient; VIQ, verbal intelligence quotient; PIQ, performance intelligence quotient; BMI, body mass index; EDI-2, eating disorders inventory-2; BDI-2, beck depression inventory-2; STAI, state trait anxiety inventory

Table 4. WMS-R results

	AN-R		Control		t	p	Cl
	Mean	SD	Mean	SD			
Age	31.44	15.65	33.50	10.61	-0.31	.759	-16.07, 11.96
Education year	11.89	1.76	14.00	1.51	-2.63	.019*	-3.82, -0.40
BMI	12.08	1.18	20.22	1.81	-11.10	.000**	-9.71, -6.58
MIQ	88.11	12.47	106.88	8.54	-3.57	.003**	-29.97, -7.56
Verbal MIQ	92.78	17.54	103.75	10.17	-1.55	.142	-26.06, 4.12
Visual MIQ	96.89	9.49	112.13	5.57	-3.97	.001**	-23.43, -7.05
AC	93.11	18.70	114.88	14.96	-2.63	.019*	-39.43, -4.10
DR	85.89	18.76	111.38	10.61	-3.49	.004**	-41.26, -9.72

*p < .05, **p < .01

Control = 8, AN-R = 9; AN-R, anorexia nervosa restricting type; WMS-R, Wechsler memory scale-revised; MIQ, memory intelligence quotient; AC, attention/concentration; DR; delayed recall

Results are expressed as mean ± SD; Cl, 95% confidence interval

Table 5. Participant characteristics

	Participant A	**Participant B**	**Participant C**
Age	20-25	20-25	25-30
Height (m)	1.55	1.71	1.51
Weight (kg)	60.80	86.00	57.50
BMI (kg/m^2)	25.31	29.41	25.22
STAI			
State	37	34	31
Trait	39	46	33
DEBQ			
Restrained	3.10	1.41	3.80
Emotional	3.69	1.31	1.54
External	4.10	4.10	2.30
FFMQ			
Observing	26	18	25
Describing	31	24	24
Acting with awareness	28	29	27
Nonjudging	21	27	30
Nonreactivity	18	19	23

BMI = Body Mass Index; STAI = State-Trait Anxiety Inventory; DEBQ = Dutch Eating Behavior Questionnaire; FFMQ = Five Facet Mindfulness Questionnaire

Table 6. Changes to weight and psychological health before, during, and after treatment

	Participant A			**Participant B**			**Participant C**		
	Baseline	Initial weight loss (%)	Weight loss at follow-up (%)	Baseline	Initial weight loss (%)	Weight loss at follow-up (%)	Baseline	Initial weight loss (%)	Weight loss at follow-up (%)
BMI (kg/m^2)	25.31	23.56	21.77	29.65	28.08	27.09	25.22	22.98	22.46
		6.91%	13.98%		5.30%	7.91%		8.88%	10.98%
STAI scores									
State	37	22	20	34	32	24	31	39	31
Trait	39	28	20	46	39	30	33	36	32
DEBQ scores									
Restrained	3.10	4.00	4.00	1.41	4.30	3.00	3.80	3.50	4.60
Emotional	3.69	2.23	2.00	1.31	1.15	1.00	1.54	1.08	1.00
External	4.10	3.00	3.70	4.10	2.50	2.00	2.30	2.10	2.30
FFMQ scores									
Observing	26	37	37	18	20	21	25	23	30
Describing	31	32	33	24	26	27	24	27	30
Acting with awareness	28	29	36	29	29	29	27	31	34
Nonjudging	21	21	32	27	35	32	30	37	29
Nonreactivity	18	26	30	19	26	24	23	23	31

BMI = Body Mass Index; DEBQ = Dutch Eating Behavior Questionnaire; FFMQ = Five Facet Mindfulness Questionnaire; STAI = State-Trait Anxiety Inventory

Weight loss was calculated as the proportion of total body weight lost

Baseline = Session 1, Initial weight loss = Session 9. Weight loss at follow-up = 18 months after Session 9

Table 7. Basic statistics and two-way ANOVA (group × time) results

		Time		F-number		
		Pre	Post	Group	Time	Interaction
Systolic blood pressure	DW	114.57 (4.63)	110.57(4.06)	1.46	39.87**	15.41**
	Lavender	114.29(3.74)	97.14 (4.27)			
Diastolic blood pressure	DW	67.67 (4.69)	70.86 (5.27)	0.37	2.21	5.83*
	Lavender	69.43 (3.82)	63.43 (3.99)			
Pulse rate	DW	73.71 (3.58)	70.86 (2.72)	0.00	8.52*	2.63
	Lavender	77.14 (3.67)	67.14 (2.30)			
SDS	DW	32.71 (2.19)	33.71 (2.57)	0.05	3.03	7.85*
	Lavender	34.57 (2.75)	30.29 (2.54)			
STAI-S	DW	39.00 (2.65)	36.57 (2.85)	0.50	13.9*	3.16
	Lavender	38.57 (3.55)	31.71 (1.87)			
VAS-Hunger	DW	5.39 (1.21)	6.03 (1.09)	0.21	2.70	0.00
	Lavender	6.07 (1.02)	6.69 (1.00)			
VAS-Thirst	DW	4.04 (0.80)	5.21 (0.79)	0.07	3.41†	0.74
	Lavender	4.74 (1.09)	5.17 (1.05)			
VAS-Appetite	DW	6.83 (0.93)	6.86 (0.99)	0.19	3.39†	3.09
	Lavender	5.66 (1.07)	6.89 (0.92)			
Cortisol	DW	15.51 (1.12)	13.53 (1.54)	0.15	10.57**	0.02
	Lavender	14.94 (0.96)	12.77 (1.46)			

†p<.10, *p<.05, **p<.01

DW = Distilled Water; SDS = Self-rating Depression Scale; STAI = State-Trait Anxiety Inventory; VAS = Visual Analogue Scale

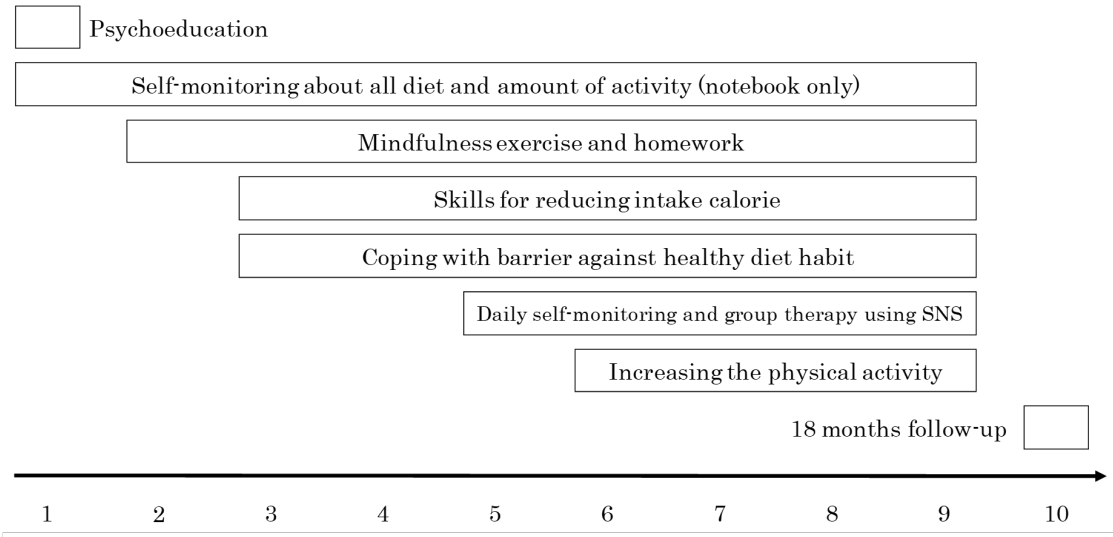

Figure 1. Overview of the diet program in this study. Session 1 to 4 was only face to face session. From session 5, participants were required to upload daily food photographs to SNS page. Session 10 was follow-up session, the distance from session 9 to 10 was 18 months

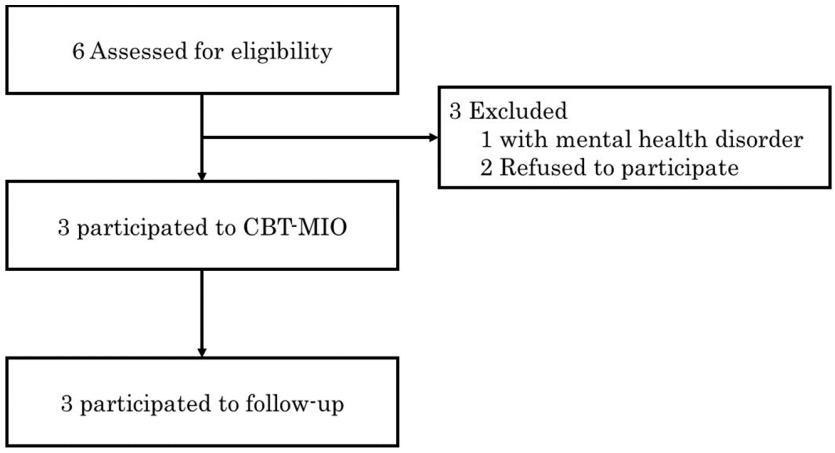

Figure 2. Flow of participants through the pilot study

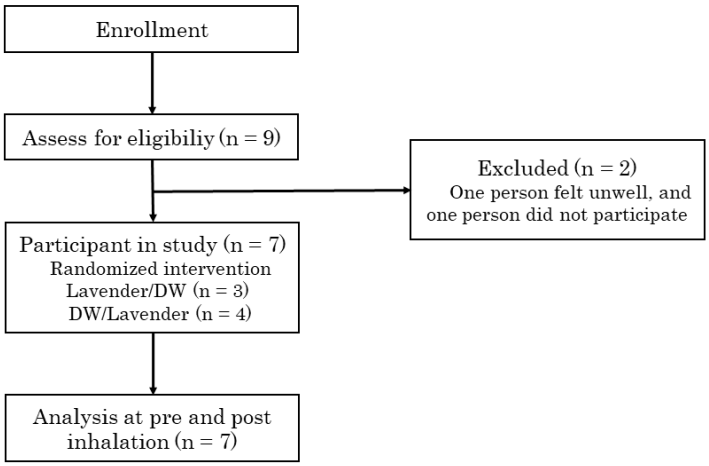

Figure 3. Flowchart of the randomised and crossover pilot trial involving healthy males
DW: distilled water

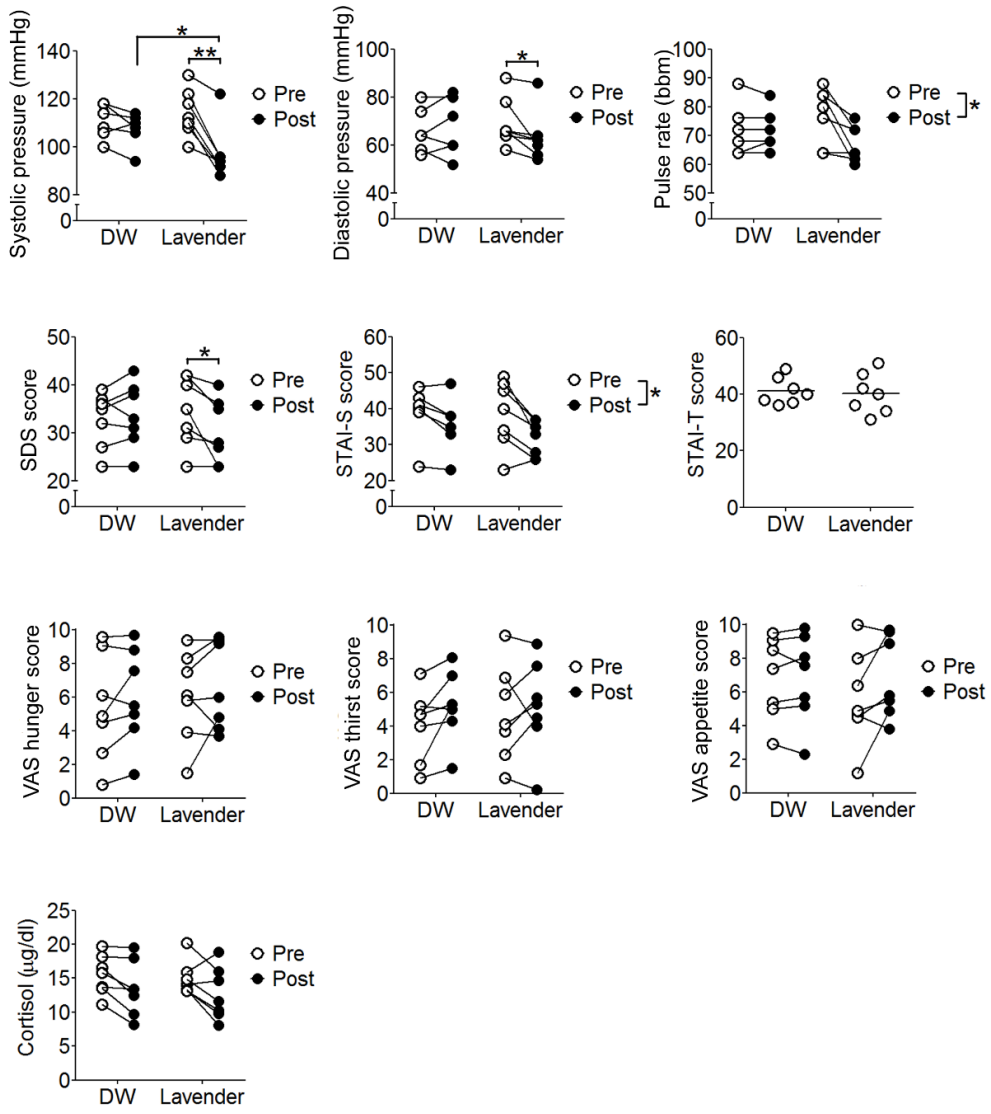

Figure 4. Effects of inhalation of lavender essential oils on systolic and diastolic blood-pressure, pulse rate, Self-rating Depression Scale (SDS), State-Trait Anxiety Inventory (STAI-S, STAI-T), Visual Analogue Scales (VASs; hunger, thirst, and appetite), blood cortisol levels in the peripheral blood of the participants, and distilled water (DW)