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The Effects of Subtle Scent of 1, 8-Cineole and (-)-Bornyl acetate on Mood, Cognition, and Behavior in the Elderly

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Abstract

This study explored the effects of subtle scents of 1,8-cineole and (-)-bornyl acetate on mood, cognition, and behavior in healthy individuals and elderly residents of nursing homes. Three experiments were conducted involving short- and long-term exposure to these scents to assess mood, memory, and task completion. Results from experiments with healthy individuals indicate that (-)-bornyl acetate improves mood, particularly for those who like the scent, whereas 1, 8-cineole improves mood, regardless of scent likability. Prolonged exposure to both scents, even at low concentrations, yielded different effects compared to no scent, such as sustained concentration of 1,8-cineole and drowsiness with (-)-bornyl acetate. In experiments with older adults, although the participants did not perceive scents, improvements in cognition, behavior, and sleep were observed. However, challenges have arisen, such as the caregiver's hypersensitivity reaction to 1,8-cineole, highlighting the need for careful consideration when implementing aromatherapy in nursing facilities. This study underscores the potential benefits of aromatherapy in improving the quality of life of the elderly. Furthermore, it emphasizes the importance of controlling scent distribution and considering individual sensitivities.

Keywords: 1,8-cineole; (-)-bornyl acetate; short-term exposure; long-term exposure; nursing home

Introduction

The efficacy of essential oils has been suggested to play a significant role in improving the quality of life (QOL) of elderly individuals. Aromatherapy, the use of essential oils derived from plants, has a strong biological and psychological influence by interacting with the olfactory system. Scent-induced changes in mood and cognition and the autonomic nervous system are intricately linked. For example, calming scents such as pine essential oil activate the Parasympathetic Nervous System and promotes relaxation and reducing stress. On the other hand, the refreshing scent such as eucalyptus essential oil activates the Sympathetic Nervous System and enhances alertness and energy. These effects of essential oils are generally considered to be influenced by an individual's preference for the scent, and subjective liking of a scent is essential to amplify the physiological and psychological benefit of the scent [1]. However, approximately 40% of the elderly people have diminished olfactory function [2]. How effective is aromatherapy for elderly people with a weakened sense of smell?

Among the numerous studies focusing on the effects of aromatherapy for the elderly, Goto et al. experimented with a subtle scent of 1,8-cineole, exposing 40 patients with dementia for an extended period [3, 4]. This study proved that a subtle scent at an imperceptible level could be effective after prolonged exposure. However, challenges remain in using 1,8-cineole due to its awakening effects; certain participants become unable to sleep at night and exhibit increased aggression [5]. Therefore, this study aimed to explore the effects of different subtle scents on cognitive function and behavioral symptoms during the day and night using 1,8-cineole and (-)-bornyl acetate. Whereas 1,8-cineole is the refreshing scent which can activates the Sympathetic Nervous System, (-)-bornyl acetate is the calming scent stimulates the Parasympathetic Nervous System. The relaxing effect of (-)-bornyl acetate has already confirmed in the author's previous research [6].

1,8-Cineole is the main component of Eucalyptus globulus Labill (E. *globulus*), which belongs to the Myrtaceae family. [7]. It has also been used to regulate and activate various systems, such as the nervous system, and to treat neuralgia, headaches, and fatigue. Henmi et al. showed that 1,8-cineole masks odors and deodorizes them by reducing the concentration of malodorous gases, and has high antibacterial activity in suppressing airborne microorganisms [8]. (-)-Bornyl acetate is one of the components of essential oils extracted from coniferous trees such as pine and fir. It has a refreshing aroma reminiscent of pine needles, often referred to as the "scent of forests." Research has demonstrated that the inhalation of bornyl acetate is effective in improving sleep quality; however, it could decrease work efficiency [9, 10].

This novel study aimed to examine the effects on improving the quality of life and cognitive function in the elderly by using subtle scents of 1,8-cineole, which has awakening effects and has been shown to improve cognitive function, and (-)-bornyl acetate, which improves sleep quality and relaxes the autonomic nervous system. Following the study on olfactory adaptation by Hirose (2019), "short-term exposure" is defined as over 5 minutes but within 10 minutes, which is the duration until physiological effects from the scent are felt and olfactory adaptation occurs, and "long-term exposure" is defined as exposure beyond 10 minutes. In addition, "subtle scent" is defined as the level of scent that is not perceived by more than 30% of healthy people. Before exposure to the elderly, two preliminary experiments were conducted on healthy individuals to examine the effects, preferences, and awareness of the aromas of 1,8-cineole and (-)-bornyl acetate and the differences in effects based on subtle concentrations. Experiment 1 involved short-term exposure of 52 healthy individuals to perceptible scents. In contrast, Experiment 2 involved the long-term exposure of subtle scents using aroma pendants on a total of 54 healthy individuals. Experiment 3 was conducted as a long-term exposure experiment with subtle aromas using aroma pendants and sticks on 30 residents of a special elderly nursing home in Nagasaki Prefecture.

Materials and Methods

All methods of the three experiments were carried out in accordance with the Declaration of Helsinki. All three experiments in

this study were approved (approval number #R4-1) by Nagasaki University Ethical Committee on September 8, 2022. Informed consent was obtained from all subjects or their legal guardians. 1,8-cineole and (-)-bornyl acetate used in the three experiments were the product of Tokyo Chemical Industry Co. LTD (TCI). The POMS used in this study was a shortened Japanese version of POMS2 published by Kaneko Shobo [10] Qualification #0912 is registered for purchase. Details of the other tests, questionnaires, and equipment used in this study are as follows.

Experiment 1: Short-Term Exposure of Perceivable Scents on Healthy Individuals

The purpose of Experiment 1 was to clarify the effects of the two scents on moods and preferences among healthy individuals. Experiment 1 was conducted in the classrooms of the Environmental Science Building at Nagasaki University. The participants were 52 healthy college students (average age 21.2), including 24 men and 28 women. The details of the scents were not disclosed to the participants, and the experiment was conducted as a single-blind study. To assess the effects of scents, Experiment 1 used 1) a questionnaire, 2) a shortened version of the Profile of Mood State (POMS) tests, and 3) memory tests. A questionnaire was used to evaluate the preference for the scent on a 5-point scale, measuring the liking or disliking of the scent. POMS is a test to measure the change in mood which classifies mood into six subscales: "tension," "depression," "anger," "fatigue," "confusion," and "vigor," and evaluates respondents' mood based on 30 questions. The memory test was a small quiz to memorize 25 words in one minute to measure changes in cognitive function [12].

Two adjacent, well-ventilated classrooms were prepared for this experiment (Figure 1). The scent was diffused using two essential oil diffusers at opposite corners of the room. Thirty minutes before the start of the experiment, the windows were closed and two essential oil diffusers began burning the scent in one classroom. The air collected by the air collection pump and the absorption tube; Tenax® TA glass TD tube (Gerstel, Mülheiman der Ruhr, Germany) for 30 seconds in the classroom after 30 minutes of operation of the diffusers with 1,8-cineole contained 667 μg/m^3 and the air after 30 minutes of operation of the diffusers with (-)-bornyl acetate contained 597 μg/m^3. For one session of the experiment, the participants first spent time in the odorless classroom and took the first POMS and memory tests. Participants spent approximately 5 min in the odorless classroom completing these two tests. Subsequently, they were moved to a room with the scent. After 3 min of quiet time, they answered a questionnaire about the scent and then took the second POMS test and the second memory test. Participants spent approximately 10 min completing one session in the scented classroom (Figure 2). All participants underwent two sessions: one for 1,8-cineole and the other for (-)-bornyl acetate. To avoid order effects, two sets of experimental sessions with different scent orders were scheduled: 1. 1,8-cineole (-)-bornyl acetate; and 2. 1,8-cineole (-)-bornyl acetate. The participants were randomly divided into two groups of 26 (12 men and 14 women) and assigned to one of the sessions.

Figure 1: Classroom used for the experiment

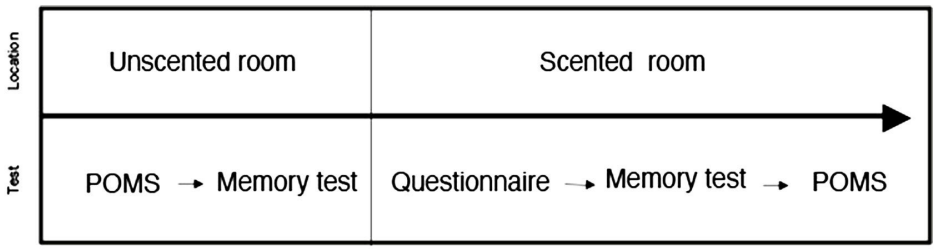

Figure 2: Experiment 1 procedure

- Memory Test (Figure 3-A): In this test, participants memorize 16 words within one minute and then write them down within another minute, providing a simple measure of memory. Since there were participants from China, a single Chinese character was used. Participants were allowed to write either Chinese characters or phonetic transcriptions. If written characters or phonetic transcriptions were incorrect, no points were awarded, and the total score was used as the evaluation criterion.

- Scent Questionnaire (Figure 3-B): The questionnaire comprised three questions; 1. Do you know this scent? (Yes, No), 2. What do you think about the intensity of this scent? (1. Too strong, 2. Strong, 3. Fair, 4. Weak, 5. Too weak), 3. Do you like this scent? (1. Very like, 2. Like, 3. OK, 4. Dislike, 5. Very dislike).

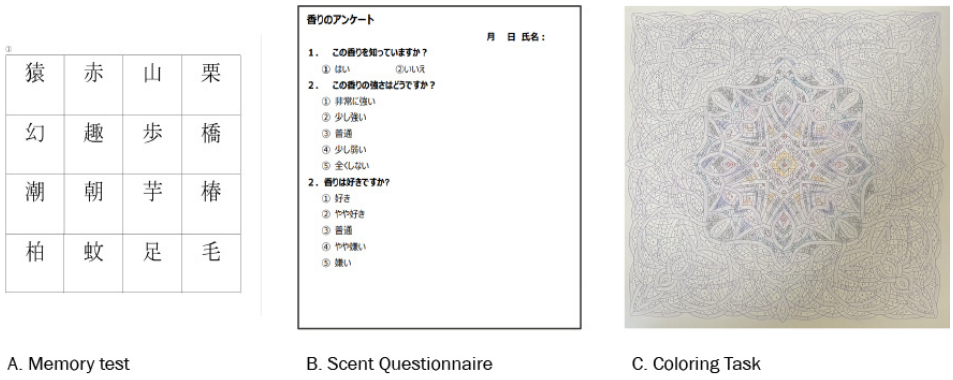

Figure 3: Tests sample

Experiment 2: Long-Term Exposure of Subtle Scents on Healthy Individuals

To assess the effects of the scents, Experiment 2 used 1) a questionnaire, 2) shortened versions of the POMS tests, 3) a memory test, and 4) coloring tasks. The process of one session of the experiment is as follows. When participants arrived at the room for the experiment, they took the first POMS test and the first memory test, then they wore an aroma pendant and answered the questionnaire about the strength of the scent of the aroma pendant. Next, they engaged in a coloring task for 20 minutes while wearing the aroma pendant. After 20 minutes, the participants took the second memory test. After completing the second memory test, participants resumed the coloring task for another 15 minutes, then took the second POMS test and the third memory test. The participants spent in the classroom approximately 60 minutes in completing one session. (Figure 4)

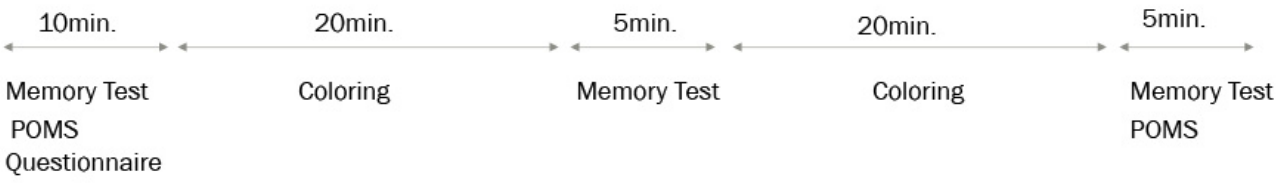

Figure 4: Experiment 2 procedure

- Coloring Task (Figure 3-C): A puzzle coloring sheet contained numbered squares, and an illustration was completed by coloring each square with a specified color according to the numbers. Three coloring sheets with different designs were obtained from the Art Puzzle Coloring Book by MDN Corporation. Each sheet contained 1000-2000 squares that needed 8–11 colors, and each took approximately 1 h to complete. In the experiment, the number of squares colored within 30 min and the completion rate were calculated to measure the work efficiency.

Experiment 3

Experiment 3 was conducted with 30 residents of a nursing home in Nozomi-no-mori [12], Nagasaki, Japan. This facility provides day care and short- and long-term stays for elderly individuals in need of care, particularly those with certified care levels of three–five, who have difficulty receiving home care. The facility is divided into six units, with each unit having ten private rooms, shared kitchens, and living spaces (Figure 5-A). The layout of private rooms typically includes a bed, bedside table, closet, shelf, and portable toilet (depending on the condition of residents) (Figure 5-B). Care at the facility was provided by seven to ten caregivers assigned to each unit, operating on a three-shift system (day shift, night shift, and part-time). Temperature control was managed by air conditioners installed in the ceiling, with settings managed by caregiving staff. Normally, windows remain closed, and doors to individual rooms are fully closed at bedtime. Additionally, as the facility prioritizes care tailored to residents' lifestyles, there are no set times for waking up, eating, bathing, using the toilet, or going to bed. No resident doctor was directly assigned to the facility, and prescriptions were not issued within the facility. Participants were recruited from three units: Units 1, 2, and 3. which consisted of individuals with an average age of 91.4, 87.8, and 89.9 years, respectively, and an average care level of 4.4 for all three units (Figure 5-C).

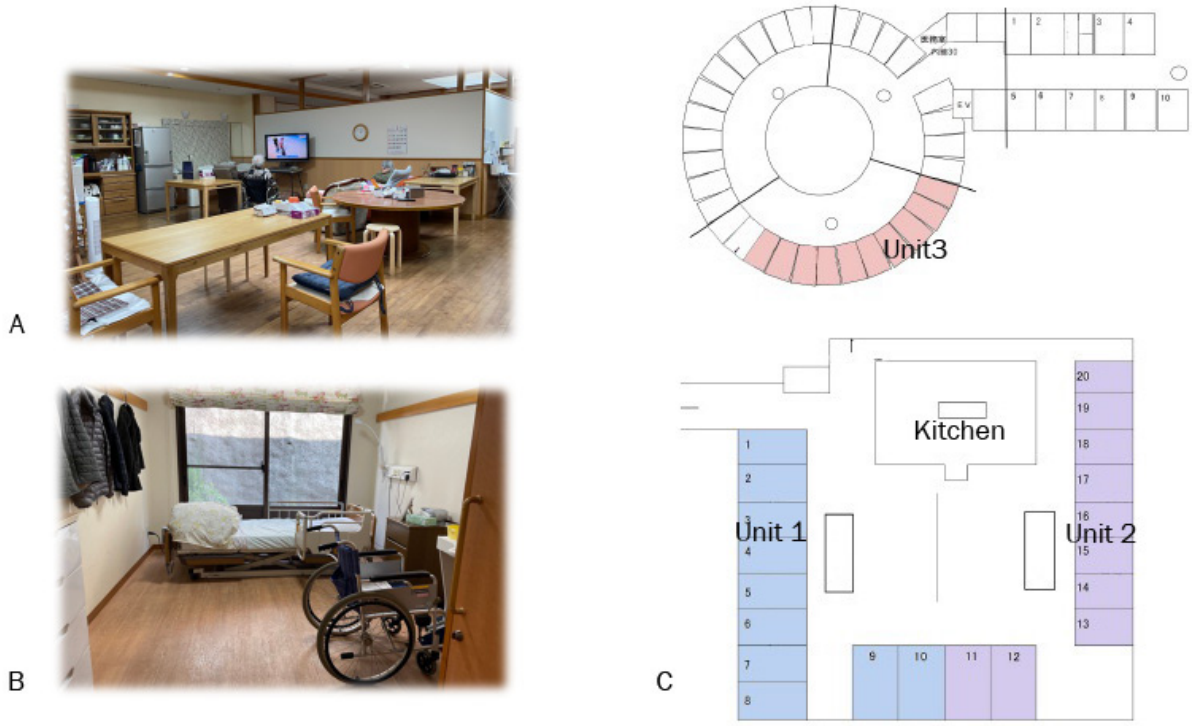

Figure 5: Nozomi-no-mori Nursing Home room and plan

The Mini-Mental State Examination (MMSE), Dementia Behavior Disturbance Scale (DBD), and caregiver reports were used to measure cognitive abilities and behaviors [13-15]. MMSE was used to assess cognitive impairment. The DBD is a scale comprising 28 items that caregivers use to assess behavioral symptoms. Two one-week experiments were conducted with a two-week washout period between the first and second experiments. Throughout the one-week experimental period, aroma pendants were used for daytime exposure, and aroma sticks for nighttime exposure. Caregivers placed the participants in an aroma

pendant at wake-up and removed it at bedtime. The aroma sticks were placed on the bedside tables of the bedrooms of participants. On examining the air collected 1m from the bedside table one hour after installing the aroma sticks, the air from the sticks with 1,8-cineole contained 2127 μg/m³ of 1,8-cineole and the air from the sticks with (-)-bornyl acetate contained 2520 μg/m³ of (-)-bornyl acetate. The participants of Unit 1 were exposed to 1,8-cineole all day during the first experiment, and to 1,8-cineole during the day and (-)-bornyl acetate at night during the second experiment. Conversely, the participants in Unit 2 were exposed to 1,8-cineole at daytime and (-)-bornyl acetate at night during the first experiment, and 1,8-cineole all day during the second experiment. Unit 3 underwent the same verification using distilled water instead of the scent. The MMSE tests were conducted in the 1st, 3rd, 4th, and 6th weeks. The caregivers completed the DBD and wrote a daily report on their findings between 14:00 and 17:00 during the experimental week (Figure 6).

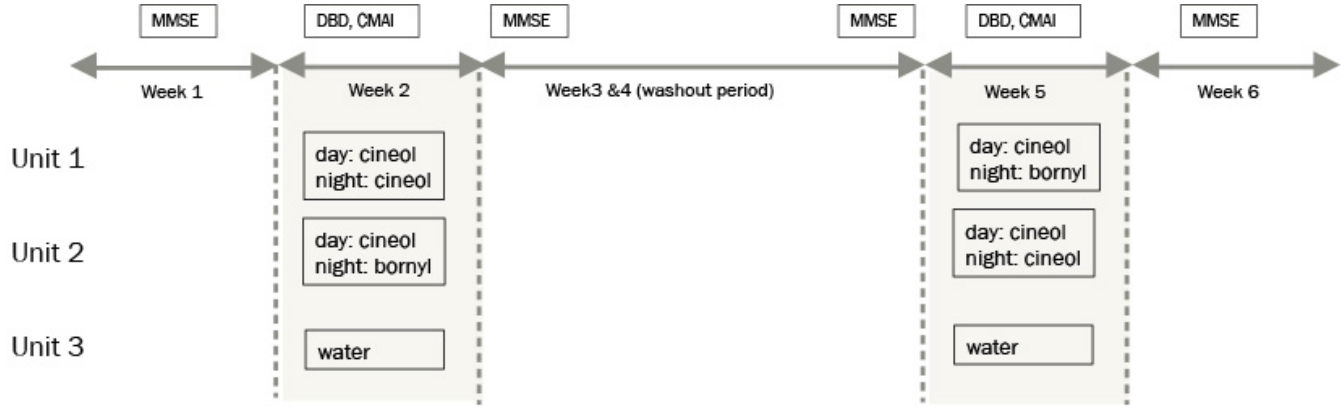

Figure 6: Experiment 3 procedure

- Caregiver Questionnaire (Figure 7): The questionnaire to be completed daily by the caregivers included three questions (1. What days and times did you care about this resident? 2. How is the mood of the residents compared to that of the previous time? (better, same, worse), 3. Please describe your observation of the residents.) below the Japanese version of the DBD evaluation table.

- Essential oil diffuser (Figure 8-A): Essential Oil Diffuser from Living Tree was used to diffuse 1,8-cineole and (-)-bornyl acetate [16]. This diffuser dispersed the essential oil particles in the air without dilution. It started operating when the button was pressed, running for 2 min, followed by a 1-minute break.

- Aroma Pendant (Figure 8-B): The aroma necklace from a Living Tree was used. A fragrance-soaked felt was stored on the pendant top and worn around the neck. The chain length was approximately 35 cm, and when worn, the distance from the top of the pendant to the nose was approximately 30 cm.

- Aroma Stick (Figure 8-B): A bottle containing 2 ml of undiluted aroma oil with two sticks inserted was used for nighttime exposure.

Dementia Behavior Disturbance Scale(DBD)
認知症行動障害尺度

以下の２８の項目について、次の０から４までの評価に従って記入してください。
０：全くない　１：ほとんどない　２：ときどきある　３：よくある　４：常にある

設問	質問内容	得点
1	同じことを何度も何度も聞く	
2	よく物をなくしたり、置場所を間違えたり、隠したりしている	
3	日常的な物事に関心を示さない	
4	特別な理由がないのに夜中起き出す	
5	特別な根拠もないのに人に言いがかりをつける	
6	昼間、寝てばかりいる	
7	やたらに歩き回る	
8	同じ動作をいつまでも繰り返す	
9	口汚くののしる	
10	場違いあるいは季節に合わない不適切な服装をする	
11	不適切に泣いたり笑ったりする	
12	世話をされるのを拒否する	
13	明らかな理由なしに物を貯め込む	
14	落ちつきなくあるいは興奮してやたら手足を動かす	
15	引き出しやタンスの中身を全部だしてしまう	
16	夜中に家の中を歩き回る	
17	家の外に出てってしまう	
18	食事を拒否する	
19	食べ過ぎる	
20	尿失禁する	
21	日中、目的なく屋外や屋内をうろつきまわる	
22	暴力を振るう（殴る、かみつく、引っかく、蹴る、唾をはきかける）	
23	理由もなく金切り声をあげる	
24	不適当な性的関係を持とうとする	
25	陰部を露出する	
26	衣服や器物を破ったり壊したりする	
27	大便を失禁する	
28	食物を投げる	
	合計得点	/112

アンケート
1．以前被験者を介護したのはいつですか。（○日の何時ごろ）
2．以前と比べて被験者の気分状態はどうですか。　良い・いつもと同じ・悪い
3．何か気づいたことがあれば教えてください。

Figure 7: Caregiver Questionnaire

A　B

Figure 8: Diffusers

Gas chromatography-mass spectrometry (GC-MS) analysis was performed using a 7890 A GC system (5975 C MSD) manufactured by Agilent Technologies with a thermal desorption unit (TDU) to determine the VOCs. The column was VF-624MS (0.25 mm I.D. x60m, film thickness 1.4 μm), and the column temperature was controlled as follows: 50℃ (1 min) →15℃/min.→160℃ (0min) →5℃/min. →250℃ (0min.) Helium was used as the carrier gas at a flow rate of 1.5 mL/min, and the analysis mode was SCAN. Target air was collected for 30 s. The compounds were identified using the pure standards; 1,8-cineole (98% purity, TCI, Tokyo, Japan) and (-)-bornyl acetate (95% purity, SIGMA ALDRICH, Tokyo, Japan). The concentration in the collected air ($\mu g/m^3$) was determined by using the internal standard; benzaldehyde (98% purity, TCI, Tokyo, Japan).

Results

Experiment 1: Short-Term Exposure of Perceivable Scents on Healthy Individuals

Participants who liked (-)-bornyl acetate or liked it more comprised 47% (more liked: 26%, liked: 22%), whereas participants who liked 1,8-cineole or liked it more was 39% (more liked: 13%, liked: 26%). In contrast, the participants who disliked (-)-bornyl acetate was 17% and the participants who disliked 1,8-cineole was 9%. The preference for (-)-bornyl acetate was more evenly divided than 1,8-cineole (Figure 9). Figure 10-A shows the change in TMD based on the results of the POMS tests conducted before and after exposure to the scents. TMD was calculated by summing the scores of the first five subscales (tension, depression, anger, fatigue, and confusion) and subtracting the vigor score. The TMD provides an overall measure of mood disturbance, with higher scores indicating a greater negative affect. The result of TMD indicated that both scents significantly improved the mood (1,8-Cineol: p=0.017; (-)-bornyl acetate: p=0.004). Figure 10-B shows the results for each POMS subscale. For the tension, depression, anger, fatigue, and confidence subscales, a higher number suggested a more negative mood. In the case of 1,8-cineole, a significant decrease was observed for tension (p=0.002), fatigue (p=0.016), and confusion (p=0.04), and a decreasing trend was observed for depression (p=0.08), anger (p= 0.06), and vigor (p=0.15) (Figure 4-B). In contrast, in the case of (-)-bornyl acetate, a significant decrease was observed for tension (p=0.04), depression (p=0.013), fatigue (p=0.0001), and confusion (p=0.02), and a decreasing trend was observed for vigor (p=0.07) (Figure 10-C). Figure 10-D shows the degree of mood change through the "before exposure- after exposure" value of POMS between two scents with a larger number indicating a better mood. The results showed that bornyl acetate was significantly more effective in fatigue recovery (p=0.02) and tended to be more effective in restoring depressed mood than 1,8-cineole (p=0.15). In contrast, 1,8-cineole was more effective at relieving tension (p=0.3) (Figure 10-D). The results of the memory test showed that the score after exposure to scent was significantly better than before exposure to 1,8-cineole (p=0.02); however, no significant difference was found with (-)-bornyl acetate. These results demonstrate the relaxing effect of (-)-bornyl acetate and the awakening effect of 1,8-cineole.

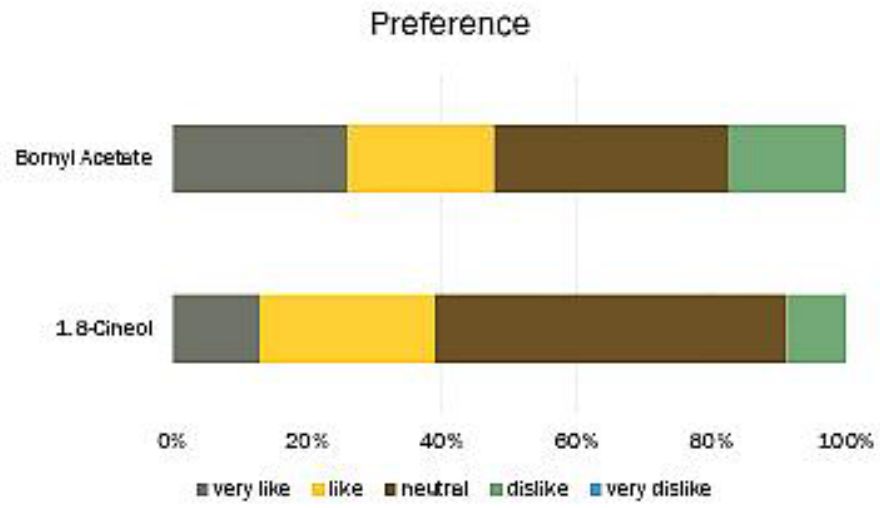

Figure 9: Preference of scent

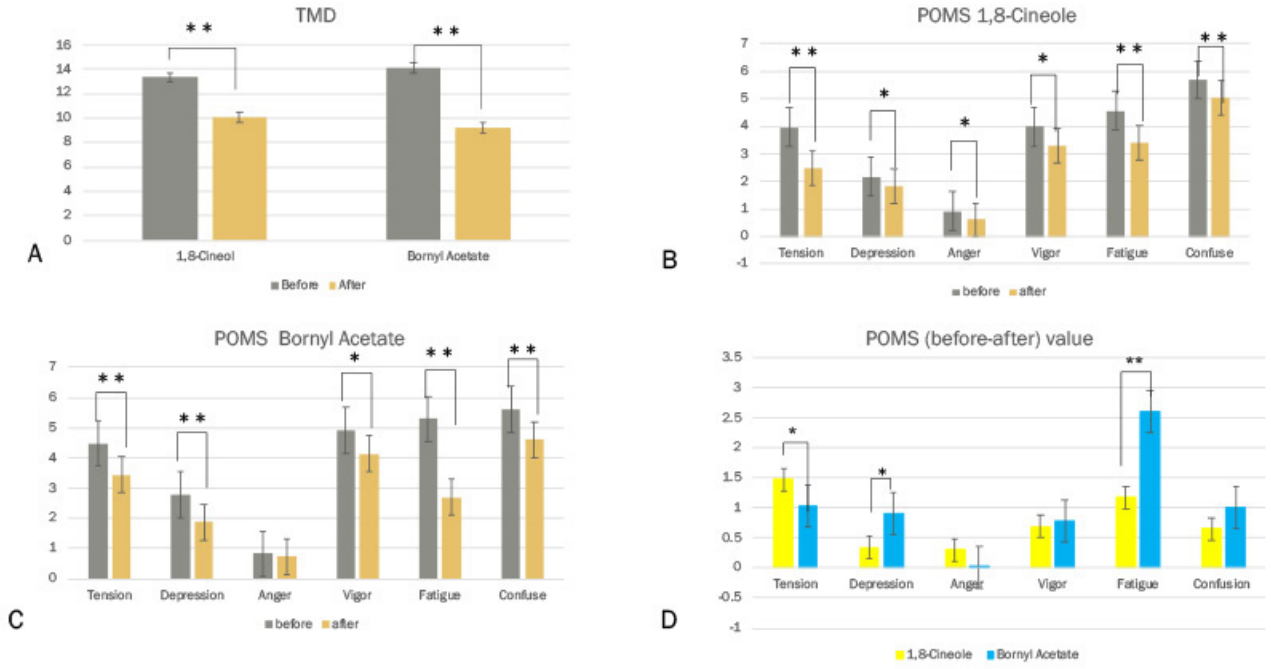

Figure 10: POMS results from short-term exposure to scent

Experiment 2: Long-Term Exposure of Subtle Scents on Healthy Individuals

Experiment 2 was conducted in a 4mx7m classroom in the Environmental Science Building at Nagasaki University. The participants were 54 healthy college students (average age 21.6 years), including 26 men and 28 women. The scent was diffused using an aromatic pendant. The participants performed three experiments wearing an aroma pendant with three different scents: 1,8-cineole, (-)-bornyl acetate, and no scent. To avoid order effects, six sets of experimental sessions with different scent orders were scheduled: 1. 1,8-cineole -(-)-bornyl acetate – odorless; 2. 1,8-cineole - odorless -(-)-bornyl acetate; 3. 1,8 odorless (-)-bornyl acetate – cineole; 4. (-)-bornyl acetate -1,8-cineole -odorless; 5. (-)-bornyl acetate - odorless - 1,8-cineole; and 6. odorless - cineole- (-)-bornyl acetate. The participants were divided into six groups of three to nine and randomly assigned to one of the sessions. The air sample was collected at a point 30 cm away from the pendant containing 1,8-cineole and the pendant containing (-)-bornyl acetate. The results of the examination of the collected air were, the air with 1,8-cineole contained 371μg/m^3 of

1,8-cineole, and the air with (-)-bornyl acetate contained 720 μg/m³ of (-)-bornyl acetate.

The result of the questionnaire on the perception of the scent from the pendant shows that the total of participants who did not perceive the scent was over 30% (-)-bornyl acetate: 39.4%, 1.8-Cineol: 34.8%), the scent from the aroma pendants was "subtle" based on the definition of this experiment (Figure 11). In the POMS test, unlike the results of Experiment 1 where TMD significantly improved with both scents, TMD showed only a trend of improvement with 1,8-cineole (p=0.5) and did not improve with (-)-bornyl acetate (Figure 12-A). This may be because the scent was weaker, the tests took longer and were more stressful than in Experiment 1, and the rate of improvement in mood was lower in Experiment 2. Looking at the subscales of POMS, in the case of 1,8-cineole, "depression" which only showed a trend of improvement in Experiment 1, had significantly improved (p=0.03). In addition, "fatigue," which had decreased significantly in Experiment 1 was on the rise (p=0.12), and "vigor," which had been on the decline in Experiment 1 increased (p=0.3) (Figure 12-B). In the case of (-)-bornyl acetate, significant improvement was seen only in "depression" (p=0.04). In contrast, "fatigue" (p=0.15) and "confusion" (p=0.28) which had significantly decreased in Experiment 1 turned into an increase (Figure 12-C). Figure 12-D indicates the degree of mood change "before exposure- after exposure" value of POMS between three scents. A larger number indicates a better mood. Though the value of some subscales increased with 1,8-cineole and (-)-bornyl acetate, results with an unscented pendant made the POMS score worse in all subscales. In addition, although (-)-bornyl acetate had a trend to have a more positive effect on "depression" than 1,8-cineole in Experiment 1, the result of "depression" is the opposite in Experiment 2. These results suggest that even a small amount of scent could have a different effect than no scent. Furthermore, the same scent could have different effects when exposed to a perceivable scent for a short period and when exposed to a subtle scent for a long time.

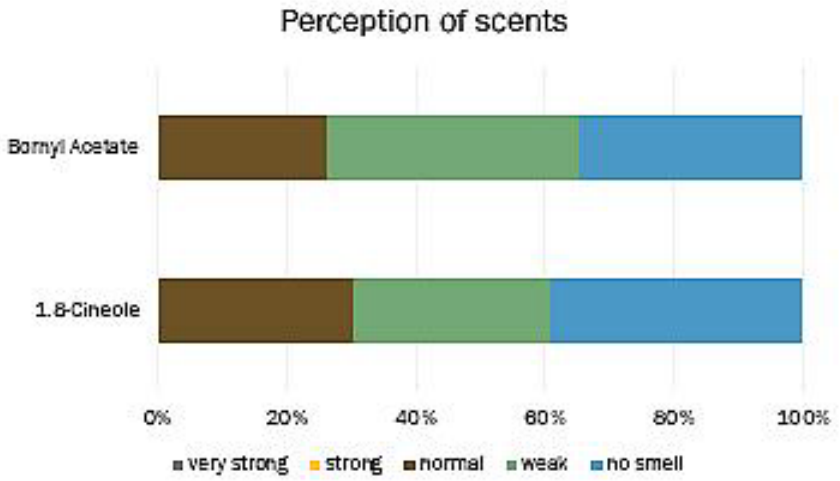

Figure 11: Perception of the scent

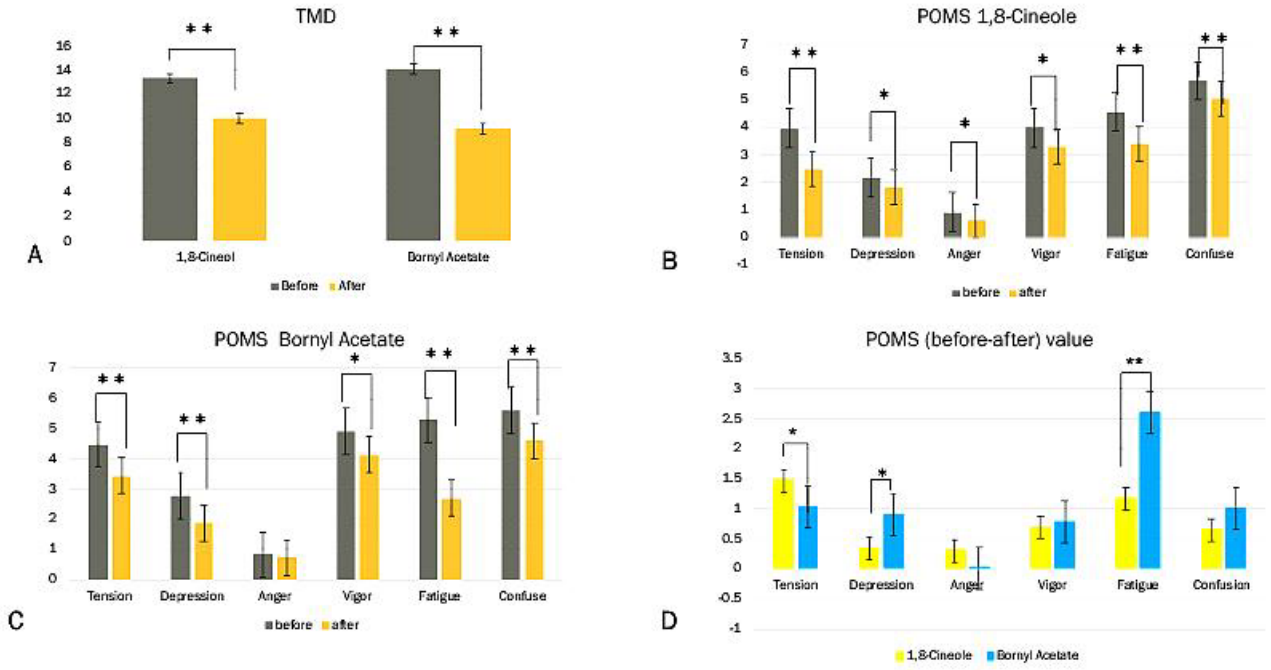

Figure 12: POMS results from long-term exposure to scent

Figure 13-A shows the completion rate for the coloring task. The completion rate with (-)-bornyl acetate was the lowest among the three conditions, and was significantly lower than that with 1,8-cineole (p=0.0007) and with no scent (p=0.009). Figure 13-B reveals a graph comparing the completion rates of the participants divided into three groups based on their likes, dislikes, and lack of perception of the scents. The graph shows that the score of the participants who disliked the scent of (-)-bornyl acetate was the lowest. With (-)-bornyl acetate, the scores of the participants who liked it were significantly higher than those of the participants who disliked it (p=0.04). The scores of the participants who did not perceive the scent were higher than those of the participants who disliked it (p=0.08). In contrast, for 1,8-cineole, the scores of the participants who did not perceive the scent and who disliked the scent were higher than those of the participants who liked the scent (p=0.46). In research on the relationship between scent preferences and relaxing effects, Akiyoshi stated that certain aromas affect mood depending on the degree of preference, whereas others affect mood regardless of the degree of preference [17]. This result shows that though the effect of (-)-bornyl acetate is related to the degree of perception, the effects of 1,8-cineole do not depend on its perception.

Figure 13-C shows the results of the three memory tests conducted in the pre-, middle-, and post-coloring tasks. The highest score was achieved with 1, 8-cineole. The score with no scent achieved the highest in the middle coloring task, with a significant increase (p=0.0002); however, it dropped to the lowest score at the end. This suggests that work efficiency decreases the fastest when working without a scent. In contrast, there was no significant difference between the pre-, middle-, and post-memory tests with (-)-bornyl acetate, however, there was a trend of decline between the middle and post-tests (p=0.49), whereas there was a trend of increase with 1,8-cineole (p=0.008). While working on the coloring task with (-)-bornyl acetate, two participants reported that they felt sleepy. These results demonstrate the relaxing effect of (-)-bornyl acetate and its suitability for nighttime use.

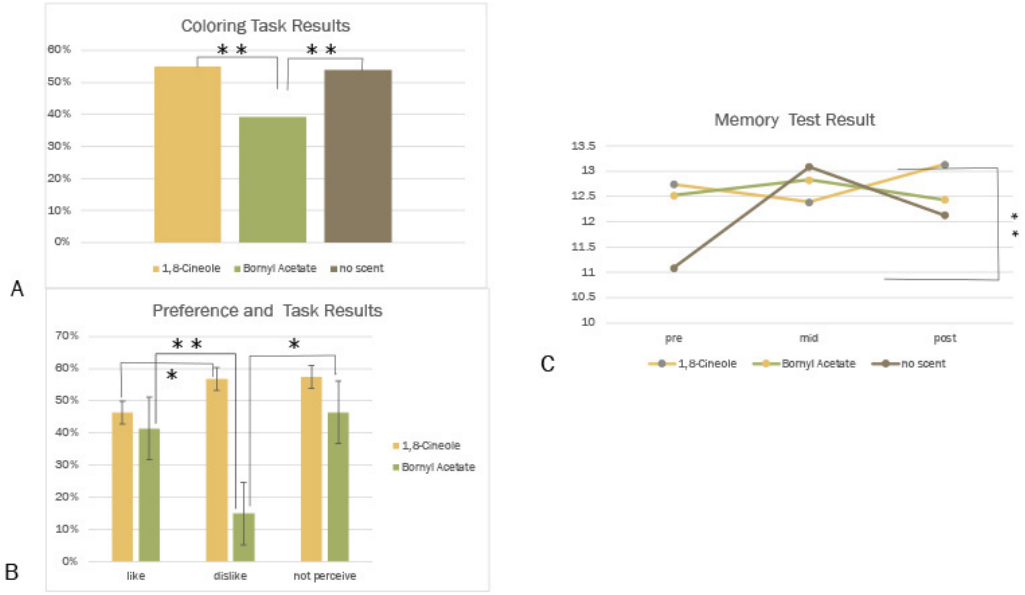

Figure 13: Coloring task and Memory test results

Experiment 3

In this experiment, as one caregiver exhibited an excessive reaction to the scent of 1,8-cineole, all the windows, which were usually closed, were opened during the day for ventilation. Consequently, the aroma did not linger, and the healthy individuals did not perceive it. Figure 14-A shows the normalized average MMSE scores of the three units. Despite these conditions, the units with scent (Units 1 and 2) showed an overall improvement in MMSE scores compared with the units with no scent (Unit 3). The MMSE scores of Units 1 and 2 did not change significantly between weeks 3 and 1; however, the MMSE score of Unit 3 decreased (p=0.08) significantly compared with that of Unit 1 (p=0.04). Although the MMSE score of Unit 3 increased between weeks 4 and 6, the average MMSE score of Unit 3 was still lower than that of Unit 1(p=0.05). Notably, when the MMSE tends to increase during the week with scents, it tends to decline during the week without scents. Hence, even if the scent was not perceived, its effects could be expected.

Figure 14-B compares the MMSE scores before and after exposure to the two scents. Between Units 1 and 2, Unit 1, which was exposed to 1,8-cineole all day during week 2, showed a significant improvement in MMSE scores between weeks 1 and 6 (p=0.03). In Unit 2, which was exposed to 1,8-cineole all day during week 5, although there was no significant difference throughout the 6 weeks, there was a tendency to improve after exposure to either scent (p=0.3) (Figure 14-B). Figure 11-C is a distribution map plotting the MMSE score difference before and after the experiment week, using the score of the week using 1,8-cineole all day as the value of the x-axis, and the score of the week using 1,8-Cineol daytime and (-)-bornyl acetate at night as the value of the y-axis. The number of points in quadrants 1 and 4 (7 points) is the number of participants who improved their MMSE using cineole all day, and the number of points in quadrants 1 and 2 (9 points) is the number of participants who improved MMSE using 1,8-Cineol daytime and (-)-bornyl acetate at night. This distribution map shows that the effect of the scent on individuals is varied; however, more individuals showed an increase in MMSE scores when exposed to (-)-bornyl acetate at night than when exposed to 1,8-cineole all day (Figure 14-C).

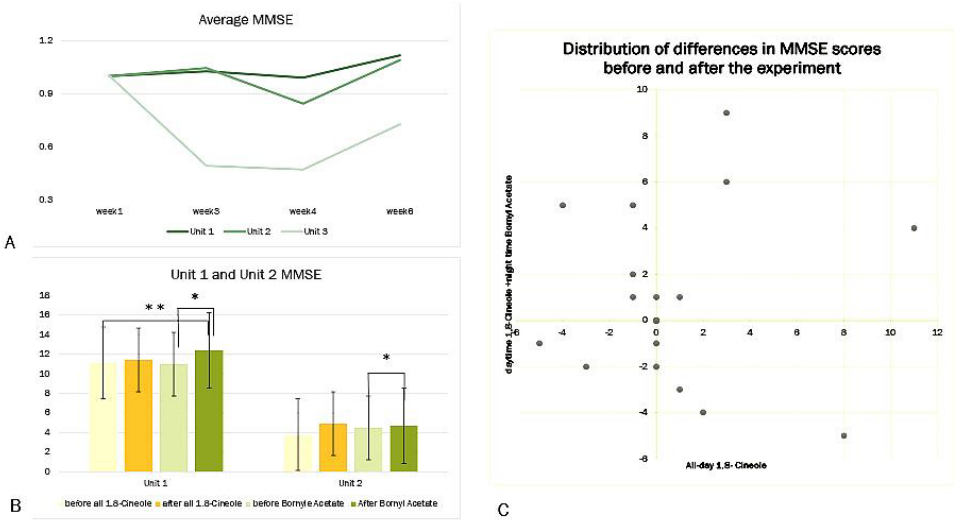

Figure 14: MMSE results

DBD showed significant improvement when (-)-bornyl acetate was used in combination with 1,8-cineole in Unit 1 (p=0.01). Among improved behaviors, improvement in “incontinence” was observed with both scents and "repeating the same thing several times" significantly improved when exposed to 1,8-cineole. In contrast, “interest in everyday matters” improved significantly when (-)-bornyl acetate was used in combination with 1,8-cineole (Figure 15). Furthermore, according to a report from the caregiver, participants in Unit 1, who were awakened during the night when exposed to 1,8-cineole all day, reported no awakening when (-)-bornyl acetate was used at night during the second week. This indicates that (-)-bornyl acetate can improve sleep quality even when the scent is not perceived.

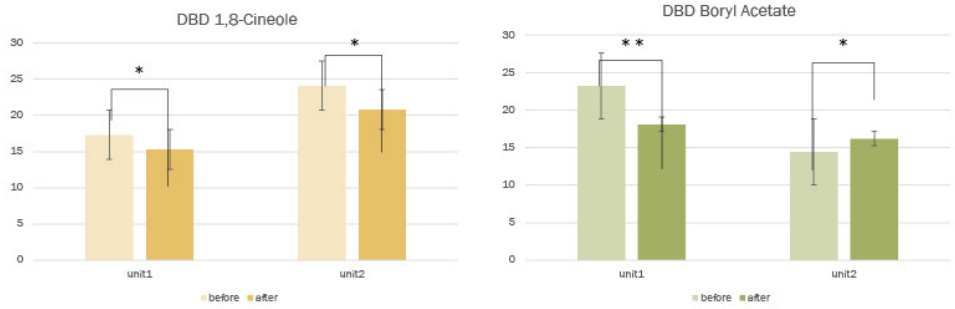

Figure 15: DBD results

Discussion

This study investigated the effects of 1,8-cineole and (-)-bornyl acetate scents at different concentrations, exposure times, and participant demographics through three experiments. From the results of experiments with healthy individuals, it was observed that the scent of (-)-bornyl acetate led to significant mood improvement in participants who liked the scent, whereas, 1,8-cineole showed mood improvement and arousal effects regardless of the scent's likability or detectability. (18) Additionally, prolonged exposure to both scents, even at low concentrations, produced different effects compared to no scent. Prolonged exposure to 1,8-cineole has the effect of sustaining concentration. In contrast, prolonged exposure to (-)-bornyl acetate induced drowsiness in participants which was observed in both healthy individuals and the elderly.

In the experiments involving the elderly, none of the participants perceived a scent. However, improvements in cognition, behavioral symptoms, and sleep were observed when participants were exposed to scents. Caregivers reported that a few partici-

pants improved their interaction with the caregivers when wearing the aroma pendant with 1,8-cineole and reported that using the aroma sticks with 1,8-cineole reduced bad odors in the room and made it easier to work. However, exposure to 1,8-cineole at night led to increased mid-sleep awakening in some participants, whereas the combined use of borneol acetate improved sleep habits. Hence, this study showed that even if the scent was not perceived, its effect could be expected with long-term exposure. The improvement in cognition and sleep observed with the combined use of borneol acetate may contribute more to the quality of life of the elderly than the use of 1,8-cineole alone.

However, one caregiver showed hypersensitivity reactions to 1,8-cineole on the first day of the experiment. Even when wearing an N-95 mask and opening all windows for ventilation, and when most people could not detect the scent of 1,8-cineole, the caregiver could not stop sneezing. During the entire week of the experiment, she suffered from an unperceivable scent leaking from the aroma pendants of participants. 1,8-cineole, a major component of many plant scents, has been known to have anti-inflammatory properties and is used in mouthwashes, cough remedies, perfumes, and cosmetics. The caregiver who was sensitive to 1,8-cineole in this experiment stated that was the first time an incident of this nature occurred and that she had never had such symptoms with tree scents or air fresheners. It was completely unexpected for anyone, including the caregiver, that the unperceivable 1,8-cineole scent would cause such an allergic reaction.

This study confirmed that combining aromatic compound with different properties during the day and at night can lead to improvements in cognition, behavioral symptoms and sleep in elderly people. However, the effectiveness of an aroma varies from person to person and even an unperceivable scent can cause excessive bodily reactions and adverse effects. This incident made it apparent that there were limitations in conducting aromatherapy in facilities with arbitrary people. Furthermore, living environments contain many aromatic compounds, controlling scent distribution is challenging when implementing aroma therapy in nursing facilities. Because this study was conducted on a limited number of residents at one nursing facility, future experiments in different environments will be necessary to confirm the results.

Limitation

This experiment was conducted in a single facility setting in Japan, so the number of subjects and individual variation were limited. It will be necessary to repeat similar experiments on more multinational subjects and confirm the results.

Author Contributions

Seiko Goto: Designed the study, directed the projects, and wrote the manuscript.

Akiko Isa: Conducted GC-MS analysis.

Kuniyoshi Shimizu: Directed the project.

Data Availability Statement

The data are not publicly available due to their containing information that could compromise the privacy of research participants. The data that support the findings of this study are available on request to the corresponding author.

Competing Interests Statement

This manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal. There are no conflicts of interest to declare.

Ethics Declarations

The three experiments in this study were approved (approval number: #R4-1) by Nagasaki University according to the Declaration of Helsinki on September 8, 2022.

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