Measurement of Olfaction in Children with Autism by Olfactory Display Using Pulse Ejection

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Abstract - Autism Spectrum Disorders (ASD) is considered as one of the developmental difficulties caused by dysfunctions of the brain. There are a variety of symptoms with ASD, but these can be significantly improved by appropriate treatment and education. Thus, it is important to find the patients with ASD while young. Recently, research on the olfactory senses of patients with ASD is being done. It is reported that there are differences of odor detection and identification abilities between people with ASD and controls. Our aim was to develop the screening examination by olfaction, hence we developed an application to assess the odor detection and identification abilities in children by using olfactory display which uses pulse ejection. We also investigated the olfactory abilities of the children with ASD using the application. However, we found some problems with application, and we made improvements. After the improvements, we assess the olfactory abilities of the typically developing children. As a result, we saw similar tendency as in the related works on olfactory abilities in children with ASD by the olfactory display.

Keywords: olfactory display, pulse ejection, autism spectrum disorders, children, interface application

1 INTRODUCTION

Autism Spectrum Disorders (ASD) is considered as one of the developmental difficulties caused by dysfunctions of the brain [1]. People with ASD have difficulties in three main areas referred to as the "Triad of Impairments" coined by Lorna Wing: impairment of social communication, social imagination, and social relation. Some examples are sudden start of conversations with strangers, difficulty in meeting their eyes, and parroting the question back. There are a variety of other symptoms with ASD, and it is not a uniform state. However, it is known that such difficulties can be significantly improved by appropriate treatment and education [2]. Therefore, it is important to detect a person with ASD while young. On the other hand, the examinations of ASD have many problems, and it is not easy to carry out an examination. Multiple staff spends time to make preparations for an examination, and it takes a long time to do an examination. For example, one examination takes a maximum of four hours in Japan, but it may take longer in other countries. Furthermore, the staffs are required to have a discussion to select the appropriate method to suit each subject's individuality. Because the examinations of ASD require such a preparation for all subjects, they are often needed to wait over one year, and the examinations cost too much money to take it lightly. In other words, no matter how much you want, it is not easy to have the examinations of ASD. There are also screening examinations of ASD, but they have some problems as well. For example, the Autism-Spectrum Quotient is unsuitable for detecting ASD while young, because it is developed for adults [3]. There is also the Modified Checklist for Autism in Toddlers (M-CHAT) as a screening examination for children [4], but the Japanese version of M-CHAT [5] has some problems likewise. It is reported that Japanese version of M-CHAT cannot detect 15% of children with ASD.

Recently, research on the olfactory senses of patients with ASD is being done. Because one of the symptoms with ASD is characteristic behavior towards odor, for example, they have a fetish for certain odors. It is reported that there are differences of odor detection and identification abilities between people with ASD and controls, hence checking olfactory abilities may make it possible to screen ASD. In this study, we assess olfactory abilities in children with ASD for developing a screening examination by olfaction.

2 OLFACTION IN PEOPLE WITH ASD

Many children with ASD have sensory difficulty [6]. For example, they don't want to get on the buses because of its odor, and they keep on sniffing certain odors. For these abnormal responses to sensory stimuli, E.Gal et al. claim that there is a change in symptoms during puberty, and in responses to sensory stimuli as well [7]. The studies on changes in symptoms with age have not been done much, but there have been reports that the symptoms were improved or more sever as people with ASD get older. Thus, it is thought that people with ASD do not show a similar trend, but the symptoms may vary according to age.

There are a variety of the symptoms of sensory difficulty, and it is reported that abnormal responses for olfaction and gustation are stronger than for vision and audition. Moreover, it is reported that abnormal responses for olfaction, gustation, and touch are stronger in the case of girls than boys, and the difficulties in olfaction of girls with ASD are more serious. Thus, it is believed that many of the patients with ASD respond characteristically to olfactory stimuli, and research on the olfactory senses is being done. There are several olfactory abilities such as the odor detection ability and the identification ability. The detection ability is the ability to detect an odor. If you cannot recognize what odor it is, you only have to be able to detect

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a certain odor. The odor identification ability is the ability to select the correct odor from several choices. You have to not only detect a certain odor but match the odor and the name correctly from several choices. In the previous studies, the detection and identification abilities were mainly measured. Suzuki et al. assessed olfaction of the adults with Asperger Syndrome (AS) by using University of Pennsylvania Smell Identification Test (UPSIT) [8] in 2003 [9]. 24 participants took part: 12 men with AS and 12 control participants. Odor identification ability of participants with AS were impaired, but there was no difference in odor detection ability. Bennetto et al. focused on odor identification ability in 2007 [10]. 48 participants aged 10 to 18 took part, 21 patients with ASD and 27 control participants. They assessed the odor identification ability using Sniffin' Sticks [11], and reported impaired ability of patients with ASD. There is also research focusing on pleasantness of odors. Hydlicka et al. assessed pleasantness of odors for 70 children aged around 10 years old (35 children with AS or high functioning autism (HFA), 35 control participants) using Sniffin' Sticks [12]. They reported that children with AS or HFA, compared to controls, perceived the odor of cinnamon and pineapple as less pleasant, the same was true of cloves. Dudova et al. assessed odor detection and identification abilities using Sniffin' Sticks, and relation between preference for odors and identification ability [13]. 70 children aged around 10 years old took part, where 35 were children with AS or HFA, and 35 were control participants. They reported impaired detection ability of children with AS or HFA, and compared to controls, they were better at correctly identifying the odor of orange and worse at correctly identifying the odor of cloves. As it was found that the odor of orange was favorite odor and the odor of cloves was least favorite odor for children with AS or HFA by Hydlicka et al. , they argued that the odor identification ability of children with ASD was related to pleasantness of odors. The patients with ASD have such characteristics regarding olfaction. However, the characteristics differed among age groups. As there is a possibility that the differences were caused by the change of symptoms associated with aging, it is believed that olfaction may be a physiological indicator of ASD by the age limit. Thus, by assessing olfaction in children, screening patients with ASD may be possible.

3 MESUREMENT OF OLFACTION BY OLFACTORY DISPLAY

It is important to find patients with ASD at while young. But the examinations of ASD have a variety of problems, and it is difficult to have an examination. Although there are some screening tests for ASD, they also have some problems. Therefore, it is necessary to develop an easy method to screen ASD. Because there are several characteristics of olfaction in people with ASD, we think measurement of olfaction in children will lead to screening examination of ASD. However, the current method of olfaction test in Japan requires great care; there are many tasks and takes too much time. There are also the problems of scent lingering in the air and filling the room. In addition, the current method may be tiring for children because it consists of repetition of simple tasks for a long time, and it has a possibility of measurement failure. Moreover, the odors used in the identification test are not always familiar to children. Thus, it is important to make a simpler method of olfactory test targeted at children. We therefore use olfactory display in the examination to solve these problems, and develop a screening application for children with ASD.

The screening examination we proposed is composed of the odor detection and identification tests. In the examination, we use the olfactory display using pulse ejection, which means scent is presented for a short duration. The person conducting the examination uses a personal computer (PC) to control the olfactory display, and the scents are presented simply by operating the PC. The usage of PC reduces the time and effort involved to present a scent. Since part of the operation is automatic, the person can still conduct the examination by only simple operations even if the person conducting the examination doesn't have enough knowledge about the olfaction tests. In addition, there are two application screens in our system, one for doctors to check the status and the other for children. Odor detection and identification test are composed of games manipulated by children so as not to bore them. The operations are simple, and children can manipulate intuitively using a touch panel monitor. Since the operations that doctors must do are made minimum, doctors can observe patients. We propose a screening application for children with ASD based on these concepts.

We hypothesized that odor detection ability in children with ASD is impaired and odor identification ability is not different from it in typically developing children, and assessed the olfaction in children.

4 OLFACTORY MESUREMENT METHOD

4.1 Olfactory Display for Medical Purposes

We developed an olfactory display as shown in Fig. 1. We call this display "Fragrance Jet for Medical Checkup (FJMC)." FJMC uses the technique used in ink-jet printers in order to produce a jet, which is broken into droplets from the small hole in the ink tank. This device can create pulse ejection for scent presentation: thus the problem of scent lingering in the air can be minimized. The 2D diagram of FJMC is as shown in Fig. 2. This display has one large tank and three small tanks, and one fragrance is stored in each tank. There are 255 minute holes in the large tank, and refer to the average ejection quantity per minute holes as "the unit average ejection quantity (UAEQ)", and the number of minute holes that emit scent at the same time as "the number of simultaneous ejection (NSE)." The device can change the ejection time at 667 μs intervals so the measurement can be controlled precisely. UAEQ from one minute hole on the large tank is 7.3 pL, and on the small tanks is 4.7 pL. As this display can emit a fragrance from multiple holes at the same time, the range of NSE is 0 to 127 for small tanks, and 0 to 255 for the large tank. These values determine the ejection quantity per unit time. Now, we refer to the average

Figure 1: Olfactory Display.

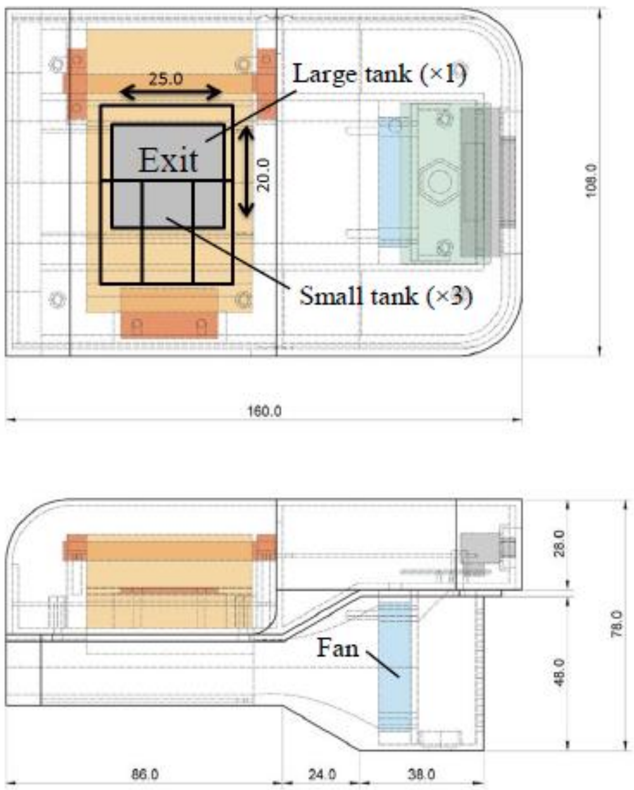

Figure 2: Plane and Side View of the Olfactory Display.

of ejection quantity from one minute hole per unit time as "the average ejection quantity per unit time (AEQUT)." Thus, it is possible to control the intensity of scent by the ejection quantity per unit time and the ejection time (ET), and the actual ejection quantity (EQ) can be calculated as follows.

$$EQ(pL) = AEQUT(pL/\mu s) \times NSE \times ET(\mu s) \quad (1)$$

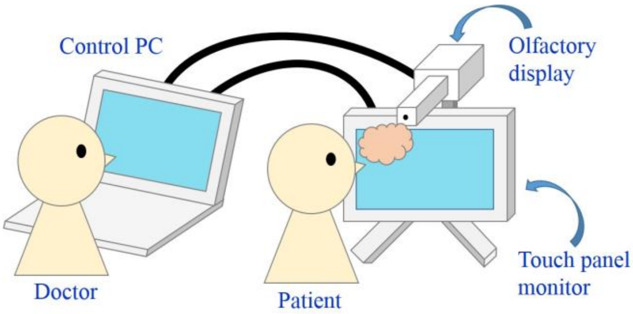

Figure 3: Conceptual Diagram.

4.2 Application for Measurement of Olfaction

We developed the screening application for children with ASD. The purpose of developing the application was to reduce the time and effort for the olfactory test and not to bore the children. We used FJMC, the PC, and the touch panel monitor in this system. Figure 3 shows a schema of the system. As FJMC uses pulse ejection, scent is emitted just short periods of time, and presented odor can be changed quickly by changing some parameters using the PC. The reason why we used touch panel monitor was to make children move their own hands. In addition, we incorporated gaming element in the olfactory test, and we also made the examination simple. The examination is composed of the odor detection and identification test. In the next section, we describe the method of use.

The odor detection test was designed as a treasure hunting game where patients try to find a smelling box out of three boxes. We used the odors of banana and pineapple, because banana and pineapple are, we thought, familiar to children. As regards the odor of pineapple, there was an additional reason. It was reported that children with AS or HFA perceived the odor of cinnamon and pineapple as less pleasant in the research of Hydlicka et al. Thus, we thought children with ASD had some characteristics regarding detection the odor of pineapple. In addition, there were four levels of intensity of the odors: 10, 20, 40, and 80. In this time, we set ET at 200ms, and the intensity was expressed by NSE. Moreover, we used only the small tanks. Detection threshold, which is the lowest intensity you can smell, was determined by using the raising method (the first intensity was 10) and three alternative forced choice procedures. There were three boxes on the screen for patients, one of them with a smell and the others odorless, and the subject select the smelling box from the three boxes. Detection threshold was determined by the intensity which the subject answered correctly twice in a row. If the subject selected the wrong answer, the intensity level was raised one level. In addition, the test was carried out firstly with the odor of banana and then the odor of pineapple. Figure 4 shows the screen for subjects. The subject pushed the arrow buttons to move the dog in front of the box the subject wanted to sniff. By pushing the button of the dog, the scent was presented and a sound rang at the same time. When the subject found the smelling box, he or she moved the dog in front of the box and pushed the "this" arrow button.

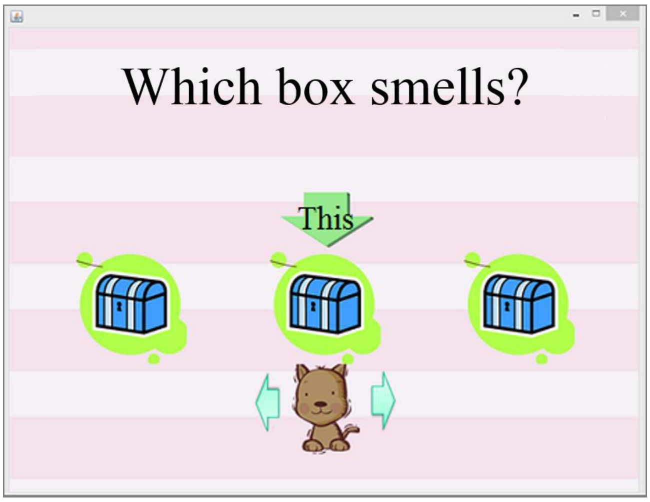

Figure 4: Odor Detection Test.

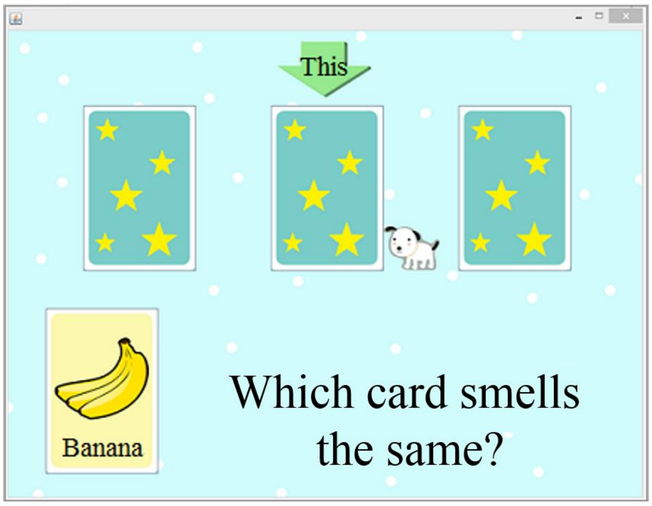

Figure 5: Odor Identification Test.

The odor identification test was designed as a card game where subjects try to find the same card by using odor as a clue. In this test, we used odors of banana, rose, and lavender. The intensity was decided by preparatory experiment, and was strong enough to sniff. Two tests were conducted in the odor identification test. Firstly, the subjects selected a card which the odor matched the illustration (Trial1). Secondly, the subject sniffed the odor of the target card, and selected a card with the same odor (Trial2). The reason why we carried out two tests was that we wanted to discuss whether the cause of impaired odor identification was the brain (the ability of associating odors and the image of odors) or simply olfaction. Both tests were carried out first with the banana and rose. In this examination, the number of correct answers was evaluated. Before the actual test, the subject checked the odor of banana and rose. The first two of the four tests were Trial1. Figure 5 shows the application screen for subjects for Trial1. The odor of banana, rose, and lavender was assigned in a random order on the three cards above. The odor was emitted by pressing the card, and the subjects sniffed the three cards to find the card with the odor matching the illustration on the bottom left. Since the goal of this test was the identification of odor and illustration, the odor was not emitted when touching the bottom left card. When they found the card with the odor

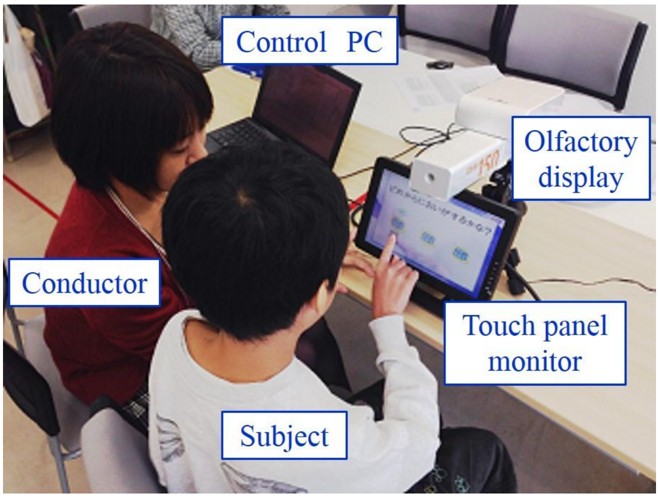

Figure 6: The State of the Experiments.

that matched the illustration, they touched the card again and the "this" arrow button to answer. After the two tests, Trial2 was conducted. Compared to the application screen for Trial1, only the bottom left card was different. Since there was no illustration on the card, first the subject had to touch the bottom left card to sniff the target odor. After sniffing the each odor for the three cards, the subject selected the card with the target odor.

5 EXPERIMENTS AND EVALUATION

5.1 Experiments for Children with ASD

The subjects were 15 patients with ASD (11 boys, 4 girls). Their ages were from 10 to 16 (mean age of 14.3 years, SD 1.74 years). We used the PC, the olfactory display, and the touch panel monitor in the experiment. The interface for doctors was displayed on the PC, and that for subjects was displayed on the touch panel monitor. The touch panel monitor was placed in front of the olfactory display so that sniffing the odor can be done while watching or touching the monitor. The experiment was conducted from 10:00 to 17:00 in a quiet room, and the subjects sat on the chair during the experiment. Figure 6 shows the experimental environment. We conducted the odor detection and identification tests, in that order.

In the odor detection test, the average of odor detection threshold for banana was 65.7 ± 55.0 and that for pineapple was 46.9 ± 44.3. However, two subjects had to do the test twice and other two subjects could not finish the test because of operation errors, so the average was calculated by excluding the two immeasurable subjects. Furthermore, the detection thresholds of the subjects who could not detect in 80 was determined as 160. In the odor identification test, we calculated the accuracy rate for each trial. The accuracy rate of banana in Trial 1 and 2 were 73.3%, and that of rose in Trial 1 was 73.3%, in Trial 2 was 60.0%. In addition, we could conduct the whole experiments within 15 minutes for all subjects. Then, we examined the olfactory senses of the subjects with ASD. The calculation was carried out by excluding the immeasurable subjects. There were no differences between the detection threshold of banana and

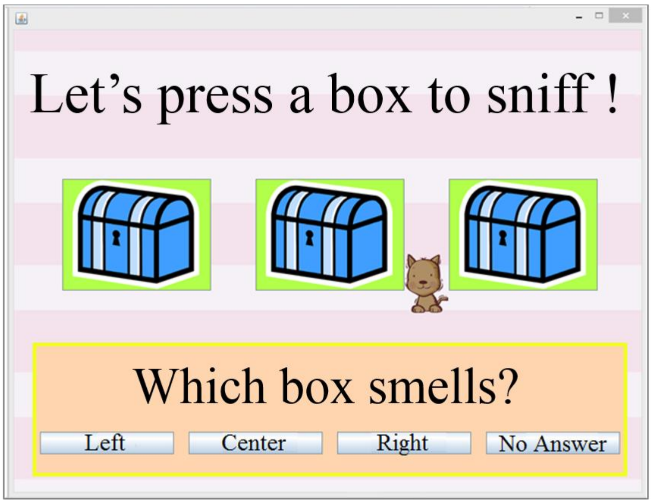

Figure 7: Odor Detection Test after the Improvements.

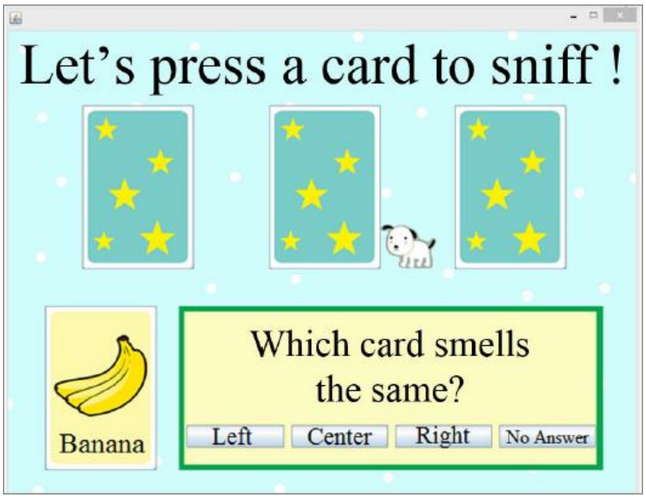

Figure 8: Odor Identification Test after the Improvements.

pineapple by the t-test ($p = 0.27 > 0.05$). Thus, it is thought that there are no differences between when using the odor of banana and when using the odor of pineapple. Next, we examined the differences between the results of identification in Trial1 (odor and illustration) and Trial2 (odor and odor) by the z-test, and we also saw no differences (banana: $p = 1.00 > 0.05$, rose: $p = 0.40 > 0.05$). Therefore, it is thought that there are no differences between the methods of two trials. We also compared the kinds of odor in Trial1 and Trial2, and there were no differences (Trial1: $p = 1.00 > 0.05$, Trial2: $p = 0.52 > 0.05$). From this results, it is thought that there are no differences between the kinds of odor as well.

5.2 Improvements of Interfaces

During the experiment, the subjects took a variety of characteristic behaviors. For example, there were many children who had shown a large interest in the touch panel monitor and the olfactory display. Some of them looked into the ejection hole of the olfactory display and stuck their nose in. In addition, they asked about the equipment very much but not so much about the operations, and the operation error was sometimes occurred in the odor detection test. Thus, we thought that it is necessary to improve the application to allow more intuitive manipulation. We also thought that it is essential that the application screen for subjects and the operation were made simpler in order to do the experiment easily for the children.

Because there were some operation errors in the odor detection test, we made improvements in the interfaces and the measurement method of the odor detection test. As regards the improvements of the interfaces, we made mainly three improvements: 1) automation of screen transition, 2) display method of the correct answer and the operation time on the application screen for doctors, and 3) adding a practice mode. Firstly, the screen control was not automatic in this application, and the doctor had to click on the "next" button to show the next screen for subjects. However, the doctor was talking with the subjects and helping them during the examination, hence the screen transition was troublesome. Therefore, the screen control was made almost automatic without the cases that the doctor should ask the subject whether the next test can be carried out. Secondly, since only the results of the tests were displayed on the application screen for doctors during the examination, they could not know which box was the correct answer until the subject selects an answer. In addition, some of the subjects took a long time to answer. We thought that there was a possibility that the operation time for the ASD group differs from that for the control group. Therefore, the correct answer and the operation time were displayed on the application screen for doctors. Finally, when describing the operation method verbally, there was no problem for the adults, but some children could not understand well without seeing the actual operations. Thus, in order to have a good understanding the operations, a practice mode was added in the odor detection and identification tests. However, the practice mode is not always conducted if the subject knows the operations. In consideration of this, we made it enabled to select the test mode, normal mode or practice mode, at the beginning of the test by doctors. The subject can run the test only once in the practice mode, and then run the test in the normal mode even if the patient selects a wrong answer.

In the odor detection test, the subjects often pushed the box or the "this" arrow button, and not the dog when they tried to sniff. So that children could make a more intuitive operation, we made the size of box bigger and the odors were emitted by touching the box. From this improvement, the time and effort for moving the dog to the box subjects want to sniff was not required. In addition, there was no choice available when the patient couldn't detect the odor, but had to choose one box. In order to solve these problems, the "this" arrow button was eliminated, and four choices (left, center, right, no answer) were placed at the bottom of the application screen for subjects. Figure 7 shows the application screen of the odor detection test after the improvements were made. There was also an improvement of the algorithm. Since the test started from the weakest odor intensity, children who could not detect the odor often appeared to have lost interest in the examination. It was most important to conduct the whole examination with interested, hence the examination method was changed to the descending method (the first intensity was 80) in order to enhance the motivation of the children. The timing of changing the level of odor intensity was also changed. If the answer was correct twice in a row, the intensity was lowered one level. Therefore, if the answer was wrong once, the examination was finished and the last intensity which they detected twice became the detection threshold.

During the odor identification test, operation errors were not occurred. However, there was no choice available for when the subject could not find an answer as well. Thus, the “this” arrow button was also eliminated, and four choices were placed at the bottom of the application screen for subjects. Before the test, the subjects could check the odor of banana and rose but not lavender, so we modified the application so that the odor of lavender can be checked in the same section. Figure 8 shows the screen of the odor identification test after the improvement.

5.3 Experiments for Controls

The experiments were also conducted for the typically developing children using the application after the improvements. The subjects were nine children (five boys, four girls). Their ages were from 9 to 12 (mean age of 10.8 years, SD 0.916 years). The experiment was conducted from 17:00 to 21:00 in a quiet room. The instruments we used were the same as the experiments for children with ASD, and we conducted the odor detection and identification tests, in that order as well.

In the odor detection test, the average of odor detection threshold for banana was 15.0 ± 10.0 and that for pineapple was 12.2 ± 4.16. In this experiment, operation error was occurred once in the odor detection test, but there were no subjects who could not be assessed. There were also no subjects who could not detect in 80. In the odor identification test, the accuracy rate of banana in Trial 1 100%, in Trial 2 was 88.9%, and that of rose in Trial 1 and 2 were 66.7%. Although we added “no answer” to choices in the improvements, the subjects did not select the choice. Thus, the adding the choice did not affect the results. In addition, we could conduct the whole experiments for all subjects within 11 minutes including the time for description. Except for the time for description, the odor detection test could be conducted in about five minutes, and the odor identification test could be conducted in about one and a half minutes. In other words, measurement time per subject was about six and a half minutes. Then, we examined the olfactory senses of controls as well. There were no differences between the detection thresholds of banana and pineapple by the t-test ($p = 0.51 > 0.05$). Therefore, it is thought that the kinds of odor did not influence the result of detection thresholds. Next, we examined the differences between the results of identification Trial1 (odor and illustration) and Trial2 (odor and odor) by the z-test, and there were no differences (banana: $p = 0.29 > 0.05$, rose: $p = 1.00 > 0.05$). As with the children with ASD, significant differences could not be found in the odor detection ability between banana and pineapple, and in the odor identification ability between Trial1 and Trial2. In short, there were also no differences between the two trials in the case of controls. However, there were significant differences between the kinds of odor in Trial1 ($p = 0.03 < 0.05$). Although there were no differences between the kinds of odor, there was

Table 1: The results of detection threshold (M ± SD).

Group	Banana	Pineapple
ASD	65.7 ± 55.0	46.9 ± 44.3
Control	15.0 ± 10.0	12.2 ± 4.16

Table 2: The accuracy rate in odor identification test [%].

Group	Trial1		Trial2	
	Banana	Rose	Banana	Rose
ASD	73.3	73.3	73.3	60.0
Control	100	66.7	88.9	66.7

also the tendency that the accuracy rate of banana was higher than that of rose in Trial2 of the ASD group and the control group. We thought the reason for this was the subjects could remember the odor of banana easier than that of rose because banana was more familiar to human life than rose. Moreover, both odors of rose and lavender were the odor of flower. There was a possibility that the choices of answer affected the accuracy rate of rose.

We compared the result of the children with ASD and the typically developing children (Table1, Table2). The detection thresholds of banana differed significantly between the ASD group and the control group ($p = 0.006 < 0.01$), and pineapple differed significantly as well ($p = 0.02 < 0.05$) by the t-test. Thus, it can be said that the odor detection ability of children with ASD is impaired. Next, there were no differences between the identification ability of Trial 1 of the ASD group and that of the control group (banana: $p = 0.09 > 0.05$, rose: $p = 0.73 > 0.05$) by the z-test, as well as the identification ability of Trial 2 (banana: $p = 0.36 > 0.05$, rose: $p = 0.74 > 0.05$). In other words, it can be said that there are no differences in the odor identification ability between ASD group and control group. In summary, we obtained the results that the odor detection ability of children with ASD was worse compared to typically developing children, but there were no differences in the odor identification ability. From these results, we thought that the ASD group could detect the odors in the odor identification test. In other words, the ASD group could perceive odors in olfactory function during the test. We thought that the part of the brain that processes perception was immature when they were young. We also thought that the reason why there were no differences between the identification abilities of the ASD group and the control group was that the subjects were young. As the symptoms of ASD may change with age [7], there were no differences in the case of children. We thought that the odor identification ability of children with ASD would become impaired at subsequent developmental stage from the related work [8].

The current results were in line with our hypothesis, but the experimental conditions were different. To compare the olfactory abilities accurately, we should reassess children with ASD using the improved application. However, we found on previous study that there was a tendency of the odor detection threshold to be lower using the raising method than the descending method. Therefore, we expect there is the same tendency when we conduct the experiments for the children with ASD again. We could also assess the olfactory abilities of the children with ASD precisely by our olfactory display, and we obtained the similar results as in the related works [13]. As the subjects of the related work and our work were close in age, there is a high possibility that the odor detection ability is impaired in the children with ASD. However, we should assess the olfactory abilities by using other kinds of odor in order to examine in more detail if subjects can have the longer experiments. In such case, we should select the combination of odors more firmly in especially the odor identification test. Moreover, it is necessary to increase the sample size.

6 CONCLUSION

In this study, we developed the screening application for children with ASD. Since it is known that the patients with ASD have characteristics related to olfaction, we introduced the odor detection and identification test for screening ASD. The application targeted children because it is important to find the patients with ASD while young. Therefore, we incorporated gaming element in the olfactory test so as not to bore the children. Moreover, we used the olfactory display in the examination in order to minimize the problems in the current olfactory measurement method used in Japan. We conducted the experiments to assess the olfactory abilities of children with ASD using our application so as to develop the way of screening ASD. During the experiments, we found some problems with the application, and we improved the application. After the improvements, we conducted the experiments for typically developing children, and compared to the results of both groups, the children with ASD had less ability of odor detection. However, there were no differences in the odor identification ability between the ASD group and the control group. In short, we were able to see similar results as in the related works on olfactory abilities in children with ASD by the olfactory display using pulse ejection, and the result was in line with our hypothesis. In addition, we could conduct the experiments for all subjects within 15 minutes. This is very shorter than the experiment time for the existing tests. In the future, we will conduct the experiments for children with ASD and typically developing children under the same experimental conditions, and hope to contribute to the construction of the screening tests for ASD by increasing sample size.

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