Research Article

Relationships between sensory processing, aberrant behaviors and food-related behaviors in individuals with Prader-Willi syndrome

A running head: Sensory processing in individuals with Prader-Willi syndrome

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Abstract

Objective: The level of sensory processing dysfunction was examined and compared with the severity of food-related behaviors and aberrant behaviors in 102 individuals (60 males and 42 females) with Prader-Willi syndrome (PWS), including 76 patients with paternally inherited deletion and 26 patients with maternal uniparental disomy within the 15q11-13 region.

Methods: The Japanese version of the Short Sensory Profile (SSP-J), the Food Related Problem Questionnaire (FRPQ) and Aberrant Behavior Checklist Japanese Version (ABC-J) were administered to PWS patients.

Results: Based on the results of SSP-J, the patients in this study were classified as follows: 27 individuals with Typical Performance, 45 with Probable Difference and 30 with Definite Difference. Among the three groups, one-way analyses of variance (ANOVAs) were conducted to investigate differences in scores of FRPQ and ABC-J. No significant differences were found in the total scores and three subscores of FRPQ. On the contrary, statistically significant differences were found in the total score as well as five subscores in the ABC-J. Post-hoc Tukey's tests revealed significant differences of aberrant behaviors in the total score and all of the five subscores of the ABC-J. Definite Difference was more than Probable Difference and

Typical Performance.

Conclusions: Approximately three quarters of individuals with PWS demonstrated abnormalities in sensory responsiveness. In terms of the relationships of sensory processing with other behavioral symptoms, aberrant behaviors and food-related problems brought out a sharp contrast; the former showed significant associations with sensory processing, whereas the latter did not.

Key Words: Prader-Willi syndrome, sensory profile, sensory processing

1. Introduction

Sensory processing means the modulation response of an individual to detect and integrate sensations from multiple sensory systems (e.g., auditory, visual, somatosensory, tactile, taste, smell). The ability of this function is essential to allow the individual to regulate the flood of sensory stimulation from different modalities [1, 2]. To modulate sensory stimuli in an appropriate manner is vital for an individual to exclude noise stimuli and to pick out targets from the myriads of sensory inputs. Without proper functioning of sensory modulation, the individual is overwhelmed by too much stimulation and is unable to understand meaningful information from his or her perceptual experiences.

The relationship of sensory processing impairments with behavioral symptoms has been studied in a variety of developmental disorders: childhood autism [3], attention-deficit hyperactivity disorder (ADHD) [4], fragile X syndrome [5], and Williams syndrome [2, 6]. So far, four types of sensory processing tendencies have been postulated. The first type is sensory over-responsiveness in which the individual responds to sensory stimuli more sensitively than usual. The second one is under-responsiveness that occurs when the individual does not react as quickly as usual and even disregards sensory stimuli. The third one is sensory seeking behavior in which the individual purposely seeks intense sensory experiences. The last one is sensation avoiding [7]. It has been argued that problematic behaviors associated with various developmental conditions are potentially derived secondarily from the effect of underpinning impairments in sensory modulation. Therefore, the relationship between sensory processing dysfunctions and other behavioral symptoms is worth investigating in a variety of neurodevelopmental disorders.

Prader-Willi syndrome (PWS) is one of such neurodevelopmental disorders, in which there is paucity of research with respect to sensory processing disorders associated with behavioral symptoms. PWS is characterized by the four main features: neonatal hypotonia, intellectual disability, hyperphagia, progressive obesity and hypogonadism [8, 9]. The physical

manifestations of PWS include: short stature, small hands and feet, hypopigmentation and craniofacial anomalies. As a contiguous gene syndrome, PWS is attributed to a loss of expression of the paternally derived genes in the q11-13 region of chromosome 15. There are mainly two origins of the loss: a paternal deletion (DEL) of 15q11-13 found in 70% of patients, and maternal uniparental disomy 15 (mUPD; when both copies of chromosome 15 are maternally inherited) found in 25% [10-13]. The remaining 1-3% of mechanism is an imprinting defect (ID), which means a defect in the genomic region that controls the activity of imprinted genes.

Behavioral characteristics of this syndrome have been well studied. Those include food-related behaviors [14], temper outbursts [15], compulsive and ritualistic behaviors [16-18], excoriating behaviors [19, 20] and autistic-like behaviors [21, 22]. Ample evidence shows that the mUPD subtype has a higher risk for autistic-like behaviors than the DEL subtype [23-25]. Such findings in terms of the affinity of mUPD with autism spectrum disorder (ASD) suggest the existence of maternally active gene(s) in chromosome 15q11-13 [23, 26-28].

Sensory processing abilities in PWS have not been examined yet, while those in ASD have been well researched. A number of studies have shown that ASD have atypical responses to a variety of sensory modalities [29-34]. These findings have been observed in individuals with high functioning ASD [35]. For diagnostic purpose, sensory processing impairments were not included in the three core behavioral deficits: social relatedness, communication skills and the presence of stereotyped behavior. Eventually, they were listed as parts of criterion B termed ‘RESTRICTED, REPETITIVE PATTERNS OF BEHAVIOR, INTERESTS, OR ACTIVITIES AS MANIFESTED BY AT LEAST’ in the newest edition of the DSM-5 [36]. Nevertheless, sensory modulation difficulties can be the first noticeable signs for parents to recognize in their children with ASD. As Ben-Sasson et al. [37] confirmed, the early emergence of sensory processing dysfunction in toddlers often indicates that such disorder grows to influence a child’s adaptive behaviors from an early stage of development. Individuals with PWS that have sensory

processing difficulties would imply the possibility of a positive relationship between sensory modulation impairment and the severity of social maladaptive behaviors in this syndrome.

For the first time, this study will survey the broad range of sensory processing ability in individuals with PWS. This study has mainly three objectives. The first is to explore the overall picture of sensory profiles in PWS and to illuminate how frequently the sensory profile differences occur in individuals with PWS and which domains of sensory processing (e.g. tactile, taste/smell, movement, auditory) are considered impaired. The second is to examine the differences between DEL and mUPD and those between female and male in terms of sensory processing impairments. Lastly, the level of sensory processing dysfunction is to be compared with the severity of other behavioral symptoms, such as food-related behaviors and aberrant behaviors.

2. Subjects and Methods

Before starting this study, the Institutional Review Board of Dokkyo Medical University assessed and approved that all procedures conformed the World Medical Association Declaration of Helsinki (No. 21107). Informed consents for behavioral and psychiatric assessment and those specific for cytogenetic and/or molecular-genetic studies were obtained from participants or their parents.

2.1 Subjects.

This study enrolled 102 Japanese participants with PWS recruited from the Departments of Pediatrics and Psychiatry, Dokkyo Medical University Saitama Medical Center. All patients were diagnosed with PWS using fluorescence in situ hybridization or the methylation test. The participants consisted of 60 male individuals and 42 female individuals, including 76 patients confirmed to having a DEL involving 15q11-13, and 26 patients confirmed to having mUPD of chromosome 15 (Table 1).

2.2 Methods

The Assessment of Behavior

Before the assessment of behavior, a Japanese version of the Wechsler Intelligence Scale [38-41] was administered for the measurement of IQ (WISC-Ⅲ, WAIS-Ⅲ).

A comprehensive set of behavioral assessment was used in terms of sensory profile, food-related problems, and aberrant behaviors. The psychologist (H.O.) who took data was not informed of the genetic status of each patient. In order to complete data taking, HO had 3 to 6 sessions for each participant. Behavioral assessments applied in this study were originally constructed on the assumption that they were applied as self-administered or informant-based scale. However, some parts of the questionnaire instructions are difficult to understand for participants and parents. Hence, H.O. administered all behavioral measures in face-to-face interview of the individuals or the parents of the PWS patients, immediately before checking for completeness and accuracy. In consequence, the quality of data gathered in this study was expected to be better than that gathered by means of mail-out survey of a questionnaire battery.

Sensory Profile

Sensory processing ability of all participants were examined by means of the Japanese version of the Short Sensory Profile (SSP-J) [42]. SSP-J consisted of 38 questions, caregivers were asked to grade the frequency that their child showed sensory processing behaviors on the basis of a five-point Likert scale (*always, frequently, occasionally, seldom*, or *never*) [43]. The questionnaire included seven subscores: Tactile Sensitivity, Taste/Smell Sensitivity, Movement Sensitivity, Underresponsive/Seeks Sensation, Auditory Filtering, Low Energy/Weak, and Visual/Auditory Sensitivity. A higher total score meant a more severe impairment. The SSP-J

has been widely used in Japan. Its internal consistency reliability of each section, including the 7 subscores and total score, in 1441 typically developing children in Japan was between 0.69 and 0.84.

The raw scores of 8 sections were converted to standardized z-scores based on the criteria proposed by McIntosh et al. [44]. In the child's responses to sensory experiences, Typical Performance was defined as z-scores above -1.00, Probable Difference as those from -1.00 to -2.00, and Definite Difference as those below -2.00.

Food-related behaviors

The severity of food-related behaviors was assessed by the means of the Food Related Problem Questionnaire (FRPQ). This informant-based questionnaire was constructed exclusively for the purpose of evaluating the level of eating behaviors in individuals with PWS. FRPQ consisted of 16 items, which were divided into three subscales: preoccupation with food (P), impairment of satiety (S), and other food-related negative behaviors (N). Examples of the questions included: "How often does the person compare the size or content of their meal with others?" (P); "After a normal sized meal, how often does the person say they still feel hungry?" (S); and "If given the opportunity, how often would the person 'help themselves' to food which they should not have?" (N). Data was presented to show that the FRPQ has reliable psychometric properties to appraise the food-related problems in individuals with PWS [45].

Aberrant Behaviors

In order to examine the level of autistic-like repetitive behaviors and other maladaptive behaviors, the Aberrant Behavior Checklist Japanese Version (ABC-J) [46] was administered to all participants. This consisted of a 58-item checklist that took about 10-15 minutes to fill in. All items were classified into five categories: a) irritability and agitation, b) lethargy and social withdrawal, c) stereotypic behavior, d) hyperactivity and noncompliance, and e) inappropriate

speech. The ABC was found to be an effective tool to identify behavioral manifestations in individuals with intellectual disability [47] and autism spectrum disorder [48]. This tool was also used for the purpose of measuring treatment response [47, 49].

3. Results

Descriptive statistics: sensory processing difference

Based on the results of SSP-J, the participants in this study were classified as follows: 27 individuals with Typical Performance, 45 with Probable Difference and 30 with Definite Difference (Table 1). One-way analyses of variance (ANOVAs) revealed no significant differences in terms of age and IQ among these three groups.

As Table 2 shows, thirty (29.4%) individuals with PWS demonstrated clinically definite dysfunction of sensory processing. The most prominent features were found in Low Energy/Weak section (49.0% in Definite Difference and 41.2% in Probable Difference). Equally pronounced was the fact that more than half of the individuals were rated as Definite or Probable Difference in Tactile Sensitivity, Movement Sensitivity and Underresponsive/Seeks Sensation. On the other hand, profound impairment was not observed in Taste/Smell Sensitivity, Auditory Filtering and Visual/Auditory Sensitivity, for more than 60% individuals were classified as Typical Performance in these categories.

Genotypical and gender differences

T-tests were conducted to examine the differences between DEL and mUPD in terms of the raw scores of 8 sections. As Table 3 shows, significant differences were not found in any of these sections. A marginal difference was found in 'Auditory Filtering', in which mUPD showed a slight trend of impairment (p=0.06). Examining gender differences with respect to sensory processing impairments, t-tests were applied in terms of the raw scores of 8 sections. Understandably there were no differences in the total score and six among the seven subscores of

SSP-J. In regards to the section of 'Underresponsive/Seek Sensation', an exceptional gender difference was observed in that males showed more severe impairment than their female counterparts (p=0.02).

Sensory processing and food-related behaviors

To compare the level of sensory processing with the severity of food-related problems in PWS, ANOVAs were conducted to investigate differences in scores of FRPQ among three groups classified based on the SSP-J results: Typical Performance, Probable Difference and Definite Difference. No significant differences were found in the total scores and three subscores of FRPQ, such as preoccupation with food (P), impairment of satiety (S) and other food-related negative behaviors (N) (Table 4).

Sensory processing and aberrant behaviors

For assessing the relationship between sensory processing and aberrant behaviors, one-way ANOVAs were used to examine scores of ABC-J among the three groups. Statistically significant differences were found in the total score as well as five subscores in the ABC-J (Table 4). The five subscores included excitement, apathy, stereotype, hyperactivity and inappropriate speech. In all scores of ABC-J, the individuals with Definite Difference in terms of sensory processing showed the most severe impairment in aberrant behaviors. Those with Probable Difference came in second, and those with Typical Performance showed the least. Post-hoc Tukey's test revealed significant differences of aberrant behaviors as follows. In ABC-J total score and all of the five scores, Definite Difference was more than Probable Difference and Typical Performance (Fig 1).

4. Discussion

This study illuminated that approximately three quarters of individuals with PWS demonstrated

abnormalities in sensory responsiveness, as only 26.5% of the entire sample were classed as Typical Performance on the basis of the total score of the SSP-J. When seven subscores of the SSP-J were probed, the most striking feature in PWS individuals was the severe abnormality in Low Energy/Weak section, in which only 9.8% of the sample in this study were classified into Typical Performance. Even in the cases of ASD, 58.0% of the individuals showed Typical Performance in the data of Tomchek and Dunn [50], who applied the Short Sensory Profile (SSP) to 281 children with ASD. In PWS, equally severe impairment was found in Tactile Sensitivity, Movement Sensitivity and Underresponsive/Seeks Sensation, in which Typical Performance was found only in 39.2%, 42.2% and 46.1%, respectively. On the contrary, there was less impaired in Taste/Smell Sensitivity, Auditory Filtering and Visual/Auditory Sensitivity, in which Typical Performance was found in 81.4%, 64.7% and 76.5%, respectively.

Be that as it may, this study did not include individuals with ASD as a control group. It is speculated that the individuals with PWS in this study were not as severe as those with ASD in terms of the levels of sensory processing ability. This possibility is suggested by the above mentioned study conducted by Tomchek and Dunn [50]. Based on the total score of the SSP, they found 83.6% of the individuals with ASD were classified into the group of Definite Difference, 11.4% into Probable Difference and only 5.0 % into Typical Performance.

In regards to sensory processing, this study failed to find significant differences between DEL and mUPD genetic subtypes and those between male and female. The sole exception was gender difference in Underresponsive/Seek Sensation section, in which male individuals were more severely impaired than female individuals. Nonetheless, these findings obtained by rough analyses should be interpreted with caution, because participants in this study did not sufficiently control confounding factors, such as age, intelligence, BMI and complications. Likewise, a precise probe into each of the seven subscores should be carried out based on sufficient sample size. Despite statistically insignificant, the p-value (p=0.06) of Auditory Filtering in inter-genotypical comparison was exceptionally low, as compared with those of the other

subscores (p=0.37 - 0.98). Due to the small sample size, type II error might conceal the possibility that mUPD showed a more severe impairment than DEL in terms of Auditory Filtering.

As far as the relationship of sensory processing with other behavioral symptoms was concerned, aberrant behaviors brought out a sharp contrast with food-related problems. No significant relationship was found between sensory processing and food-related behaviors. On the contrary, significant associations were observed between sensory processing and aberrant behaviors. Such a finding held true across diverse types of aberrant behaviors, including excitement, apathy, stereotype, hyperactivity and inappropriate speech. Regardless of differences in behavioral manifestations, it was observed that sensory processing abnormalities were highly linked with maladaptive behaviors. Similar findings supporting a predictive association between sensory processing dysfunction and problem behaviors have been demonstrated in ASD [51, 52]. In this respect, the current study is the first report to confirm the significant relationship between sensory processing dysfunction and problem behaviors in PWS.

Questions remain unanswered whether sensory processing impairments are a component of core behavioral symptoms or the concomitant phenomenon. Even in ASD, a debate is still ongoing whether sensory processing deficits are an essential attribute or an accidental property [53]. A systematic aggregation of evidence is needed to clarify whether sensory symptoms should be regarded as core behavioral features of PWS (i.e. temper tantrums, compulsive, ritualistic behaviors, skin picking behaviors and autistic-like behaviors).

This study found lack of significant relationship between food-related behaviors and sensory processing impairments in PWS. Such a pattern was found in maladaptive food-related behaviors, such as impairment of satiety, preoccupation with food and other food-related negative behaviors. In ASD, on the other hand, relationships have been found between variables relating to food intake and those relating to sensory reactivity. For example, Tanner et al. [54] demonstrated a positive relationship between total food eaten and SSP Taste/Smell Sensitivity

scores, and a negative relationship between limited food variety and SSP Taste/Smell Sensitivity scores. As have already been pointed out [55], abnormal eating behaviors in PWS may be derived from a dysfunction in a satiety system, but not in the form of hunger. It is suspected that sensory processing impairments do not play a significant role in the mechanisms underlying hyperphagia related to lack of satiety in PWS.

This study has some methodological limitations. First, the effect of chronological age and intelligence was not fully considered. Unfortunately, the number of participants in this study was too small to analyze sensory profile differences in multiple age and/or intellectual groups. Second, this study failed to assess the influence of endocrinological factors including growth hormone therapy, obesity and diabetes. As there is some evidence to suggest the negative impact of type 2 diabetes on sensory processing [56], the comparison between PWS individuals with and those without diabetes in regard to sensory responsiveness is of particular interest. Third, the impacts of other complications (scoliosis, cellulitis, etc.) were not examined. It has been well known that individuals with PWS have an incidence of scoliosis at rates between 40-90% [57, 58]. At the same time, orthopedics literature has often pointed out that individuals with PWS have an increased pain tolerance, which may potentially be helpful in the stage of rehabilitation after surgery [59]. Equally well known is the fact that individuals with PWS often engage in self-harming behaviors, such as compulsive skin picking and gouging. Consequently, erysipelas and cellulitis are common skin complications associated with PWS. Future research is needed to investigate the relationship between sensory processing differences and related problematic behaviors, considering the influence of orthopedic and dermatological complications.

Data Availability Statement

The datasets used to support the findings of this study are available from the corresponding author on reasonable request.

Conflict of Interests

None

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