COHORT STUDY

Facial Morphological Changes Following Denture Treatment in Children with Hypohidrotic Ectodermal Dysplasia

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Abstract: ***Purpose:*** *The purpose of this study was to characterize the facial morphology of Chinese children with hypohidrotic ectodermal dysplasia (HED) and quantify facial changes after prosthetic treatment.* ***Methods:*** *3-D facial images of 12 HED children were taken and their facial morphology was compared against 28 healthy controls. Facial changes due to denture placement were also quantified. Group differences were quantified and visualized by superimposing the average faces with robust Procrustes superimposition. Partial least square regression was used to investigate the effects of group membership (HED or controls, pre- and posttreatment) on facial morphology.* ***Results:*** *HED patients had a more prominent forehead, depressed nasal region, depressed zygomatic zone, flat cheeks, and protuberant lips and chin compared with controls. The strongest differences were localized in the middle and lower face, especially in the cheeks and zygomatic and chin regions (P<0.05). Pre- and posttreatment comparisons showed the chin retruded (P<0.05). Statistical facial differences between the posttreatment patients and the controls were localized in the perinasal area and submental region (P<0.05).* ***Conclusions:*** *The facial morphology of Chinese children with hypohidrotic ectodermal dysplasia differs significantly from healthy children, creating a more concave facial profile. Posttreatment facial changes provide a better understanding of dentures' role in improving facial appearance.* *(Pediatr Dent 2020;42(4):315-20) Received March 4, 2020 | Last Revision May 8, 2020 | Accepted May 11, 2020.*

KEYWORDS: ECTODERMAL DYSPLASIA, FACE, DENTAL PROSTHESIS, PARTIAL LEAST SQUARE REGRESSION

Ectodermal dysplasia (**ED**) represents a group of rare genetic disorders characterized by abnormal development of two or more ectodermal derivatives, including hair, teeth, nails, and certain glands.[1] Hypohidrotic ectodermal dysplasia (**HED**) is the most common form, with an estimated incidence of one in 100,000 births.[2,3] The distinguishing features include hypohidrosis, hypotrichosis, missing and malformed teeth, smooth dry skin, and periorbital pigmentation. It can be inherited in an autosomal recessive, autosomal dominant, or X-linked recessive manner. In the X-linked inheritance, typical traits—manifest apparently in males and female carriers—show variable severity, mostly from mild to moderate.[1,4] Affected individuals are often reported to have specific craniofacial traits, such as maxillary hypoplasia, mandibular prognathism, frontal bossing, and saddle nose.[5] The anterior facial growth rotation leads to a more skeletal Class III facial type over time, giving patients an aged appearance.[6] These anomalies can cause severe orofacial impairment in masticatory function and esthetics. Besides, severe facial and dental deficiencies can be a source of social and emotional distress, affecting children's self-esteem and life quality.[7] Hence, prosthodontic intervention is typically recommended in early childhood.[8]

Removable dentures are typically needed with regular adjustments and replacements in growing HED children.[8,9] This not only improves stomatognathic function but also psychosocial interactions by enhancing facial esthetics.[10,11] Understanding how facial morphology changes after treatment is important, as it is one of the targets of intervention for dentists. To date, investigations concerning the craniofacial characteristics of HED have focused mainly on the evaluation of skeletal features by anthropometry or cephalometry.[5,6,12-14] These studies found abnormal growth of the facial skeleton and, without treatment, deviation from normal controls, increasing over time. However, traditional two-dimensional cephalometrics has some limitations. First, the ionizing radiation is invasive; second, the linear distances and angular measurements used fail to represent the whole facial structure. Aside from these skeletal findings, it's unknown whether more characteristics exist in the overlying soft-tissue morphology. To date, comprehensive and quantitative studies on facial soft-tissue characteristics of HED patients remain rare.[15-17]

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Although many features of the HED syndrome have been described with linear distance or angle measurement in two dimensions (2-D), the analysis of the entire facial surface of HED has been rarely characterized in three dimensions (**3-D**), especially in Chinese subjects. Facial morphology of males with HED was previously evaluated in 3-D utilizing 24 discrete anatomical landmarks, and ethnic backgrounds included Caucasian, Hispanic, and African American.[17] However, these sparse landmarks only covered certain areas of the face and much information about the full 3-D structure of the face was lost.[18] Over the past several years, advances in surface imaging and increased computing power have made it easier to quantify the entire facial form indirectly and virtually in 3-D.[19,20] These techniques, coupled with geometric morphometric statistical analysis, make it possible to uncover subtle yet relevant aspects of craniofacial dysmorphology, which are difficult to define via traditional anthropometry or cephalometry.

The purposes of this study were to: (1) provide a comprehensive facial morphological analysis of Chinese hypohidrotic ectodermal dysplasia children using 3-D facial images; and (2) evaluate facial changes immediately after these children wear their first removable dentures.

Methods

Ethics statement. Ethical approval was obtained from the Ethics Committee of Peking University Health Science Center. Written informed consents were received from parents or guardians of all the participants before enrollment.

Participants. The HED patients were recruited retrospectively from January 1, 2014, to December 31, 2018, by two specialists in the Department of Pediatric Dentistry, Peking University School and Hospital of Stomatology, Beijing, China. Patients included in this study presented abnormalities of the following ectodermal structures: teeth, hair, and sweat glands (OMIM #305100, OMIM #224900, OMIM #129490). Twelve male patients between 66 to 120 months old (mean equals 94.8±22 [standard deviation] months old) were included. All subjects were of Chinese ancestry (Han majority). No subject had undergone any previous craniofacial surgical procedure.

The normal control group consists of 28 male children with matched age, sex, ethnic group, and body mass index. Age of the control subjects ranged from 66 to 132 months (mean equals 94.8±18 months old), with all controls being of Chinese ancestry (Han majority). They all had Class I occlusion. None of the participants had apparent facial disharmony or a medical history of congenital disease or craniofacial surgery.

Oral manifestations and prosthetic treatment. Intraoral examinations revealed that the HED children had between zero and four teeth remaining in the oral cavity, with a protuberant tongue. The remaining teeth were presented as tapered anterior teeth and widely spaced molars. The alveolar ridge is low and knife-edged (Figure 1b). Panoramic radiographs showed the absence of multiple primary teeth and permanent teeth.

All the patients had a prosthodontic treatment plan to make their first dentures at the first visit. The dentures were fabricated in heat-processed acrylic resin. As the mouth of HED children is often dry with reduced saliva flow, to obtain more adequate and acceptable fitness, denture liners made from soft diaphragms (dental diaphragm-595120, Erkoloc-Pro, Erkodent Erich Kopp GmbH, Pfalzgrafenweiler, Germany) were created as denture bases.

Facial imaging acquisition. Facial images of HED children were taken before and immediately after denture restoration. The facial images of the control group were captured during dental check-ups. The participants were instructed to maintain a neutral facial expression during imaging, with lips at rest and mouth and eyes closed to minimize involuntary movement. The full 3-D facial surfaces were captured using the FaceScan digital camera system (ISRA VISION, Darmstadt, Germany). The FaceScan system is a structured light scanner with a 0.2-mm nominal accuracy. It has a double-mirror structure that captures 3-D images from three different angles simultaneously (±0.2 seconds). In a 3-D photograph, the facial surface is represented as a cloud of points, interconnected to define an irregular polygonal "mesh" in a 3-D coordinate space.

Image processing. Existing spatially dense morphometric techniques were used to standardize the 3-D images. Instead of using sparse manually indicated landmarks, a large number of quasi-landmarks were used to represent the entire face. Correspondence between quasi-landmarks on all images was achieved by an automated mapping strategy, as described previously.[20,21] Essentially, a generic template face was warped into the shape of each image. Each face is then represented by the 8,568 quasi-landmark points of the template. Each quasi-landmark occupies the same position on a given face as on all the other faces, enabling image data from different individuals to be analyzed and compared in a spatially dense way. An open-source implementation of the mesh-to-mesh mapping algorithm is available at *github.com/TheWebMonks/meshmonk*.[22]

Facial averaging and group difference comparisons. All faces were brought into a common frame of reference using a generalized Procrustes analysis.[18] The faces were not scaled to a standard size, as the difference in size was of primary interest. The average faces of the HED patients, both pre- and posttreatment, and the controls were generated separately, by averaging each of the corresponding points on the faces, within each group. The average faces of the HED patients and the average faces of the controls were superimposed with the robust Procrustes superimposition.[18,20] Facial morphological differences

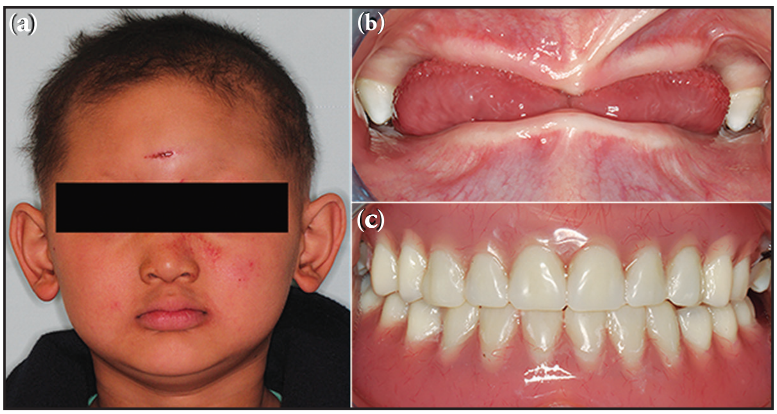

Figure 1. A hypohidrotic ectodermal dysplasia patient at five years of age. (a) Facial appearance of the patient. (b) Intraoral examination shows two tapered primary maxillary canines, a knife-like alveolar edge, and protuberant tongue. (c) Intraoral picture with removable dentures placement.

between the groups were compared and visualized using color-coded maps. The difference between the pretreatment average and the average of the controls was exaggerated to highlight the affected areas. This was done by subtracting the coordinates of the control average from the pretreatment average, multiplying this difference by two, and then adding this difference back on to the control average. The pre- and posttreatment average faces were superimposed and compared to evaluate the effect of denture placement effect on facial morphology.

Partial least square regression (**PLSR**) was used as an underlying regression model to investigate the effects of group membership (HED or controls, pre- and posttreatment) on facial morphology.[23] Unlike ordinary least-squares regression, PLSR can be used when the number of observations exceeds the number of response variables and when the response variables are highly correlated. This is the case here, due to the spatially-dense quasi-landmark data used to represent facial form. The significance of the effect of group membership on facial morphology was tested following the permutation framework for partial regression coefficients. Within this framework, effect size or R^2 was used as a test statistic, which is defined as the proportion of the total variance in facial morphology that can be explained by group membership. Statistical significance was tested using 10,000 permutations. A *P*-value of <0.05 was considered significant. The effect size and significance in each quasi-landmark were visualized on the shape of the overall average face by color-coding the points according to the values of each statistic. All statistics were implemented using custom-written code in MATLAB® R2017b (Mathworks Inc., Matick, Mass. USA).

Results

Differences between HED patients and normal controls. Figure 2 shows the difference between the average HED face and the average face of the age- and sex-matched controls. The HED patients had approximately 1.5 to 3.0 mm more prominence in the forehead than the controls, a depressed nasal root and bridge, collapsed nasal alar, depressed zygomatic zone, and flatter cheeks. The lower lip and the chin protruded (Figure 2a). The statistically strongest effects (highest R^2) were localized in the middle and lower face, especially in the cheeks, zygomatic region, and chin region. Nearly all the differences seen across the entire face were statistically significant ($P<0.05$; Figure 2b).

Figure 3 shows the average face of the controls, the pretreatment group, and an exaggerated morph of the pretreatment group to emphasize the differences between the groups. This highlighted the prominent forehead, saddle nose, protruded lips and chin, and concave facial contour of the HED patients (Figure 3a). The HED pretreatment average face is presented in Figure 3b. This showed a concave appearance similar to an elderly edentulous facial appearance.

Pre- and posttreatment changes of HED patients in facial morphology. Facial changes of HED children were seen in the cheeks and the chin region immediately after prosthetic restoration (see **Supplemental Electronic Data – sFigure 1a**). The cheeks became more prominent with a chin retrusion. Downward movement in the submental region was observed. However, only the changes in the chin were

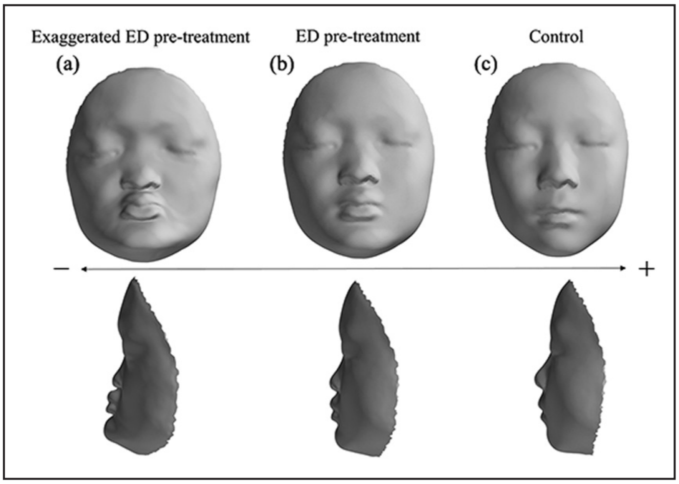

Figure 3. The exaggerated morph of the pretreatment hypohidrotic ectodermal dysplasia face. (a) Exaggerated HED pretreatment average face shows a concave profile. (b) HED pretreatment average face. (c) Control average face.

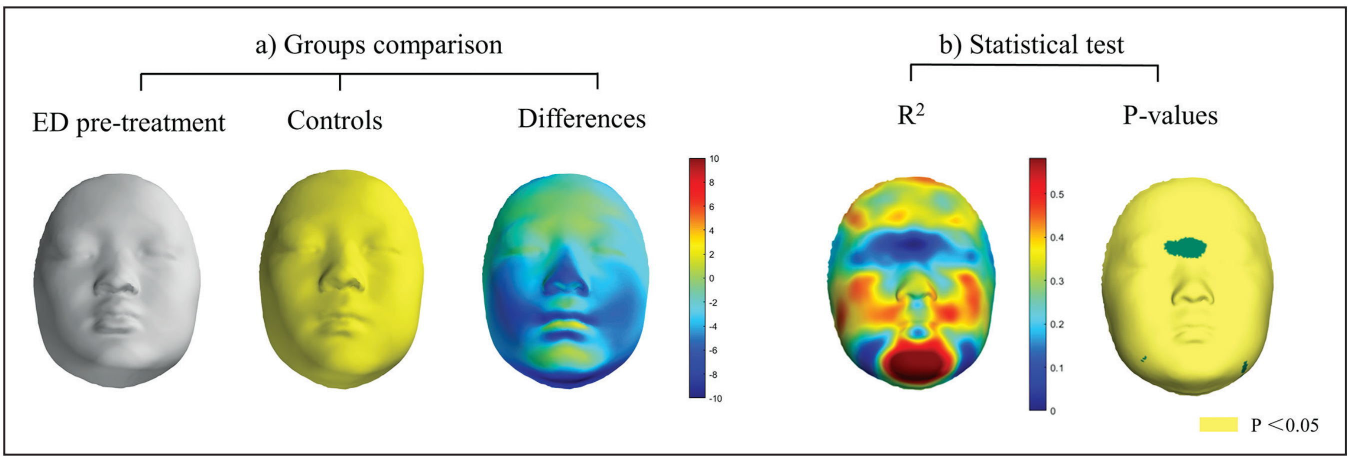

Figure 2. (a) Visualization of differences in facial morphology between the average hypohidrotic ectodermal dysplasia face and the controls. Red equals outward displacement; dark blue equals inward displacement. HED patients show a more prominent forehead, depressed nasal root and bridge, collapsed nasal alar, depressed zygomatic zone, and flatter cheeks. The lower lip and the chin protrude. (b) R^2 indicates proportion of the total variance in facial morphology that can be explained by group membership. Red equals strongest effect; dark blue equals no effect. The statistically strongest effects (highest R^2) are localized in the middle and lower face, especially in the cheeks, zygomatic region, and chin region. Statistically significant areas ($P<0.05$) are indicated in yellow.

statistically significant (*P*<0.05; **Supplemental Electronic Data – sFigure 1b**).

Differences between posttreatment HED patients and normal controls. Compared to controls (see **Supplemental Electronic Data – sFigure 2a**), the forehead of the posttreatment HED group was more pronounced. The nose (root, bridge, and nasal alar), zygoma, and cheek were more depressed. The upper lip was prominent, and the chin protruded. The statistically strongest effects (R^2) were observed in the area around the nasal wing and submental region. Whereas the largest differences were found around the perinasal area and submental region (*P*<0.05), the differences in the other areas were not statistically significant (see **Supplemental Electronic Data – sFigure 2b**).

Discussion

This is the first comprehensive study to quantify 3-D facial morphology of Chinese male HED children and facial changes immediately after prosthetic treatment. Compared with age- and sex-matched controls, HED patients had a more prominent forehead, depressed nasal bridge and alar collapse, flat cheeks, depressed zygomatic zone, everted lips, and more protruding chin. The midfacial recession suggests maxillary and zygoma hypoplasia. The lower portion of the face was reduced in height. This combination of morphological changes resulted in a more concave facial profile. Immediately after removable dentures placement, the cheeks became more prominent. Downward movement in the submandibular region and significant reduction in chin protrusion were observed. The delivery of dentures restored the fullness of the cheek and increased the vertical height of the lower face. Compared to controls, the prominence of the forehead and the concavity of the zygomatic region improved with dentures. The posttreatment changes of the upper and middle face suggest that the effects of prosthetic treatment might not be limited in the lower face. However, denture prosthesis did not lead to significant improvement in the depression on the perinasal area and the protuberance of the upper lip.

Previous cephalometric and anthropometric studies elucidated the main craniofacial characteristics of HED.[6,12,14,15] The patients were found to have midfacial hypoplasia with maxillary retrusion and retroclined nasal bone, a deeper supramental sulcus, prognathic mandible, and reduced facial height. Additionally, as found in previous reports,[13,16] the HED patients presented greater growth in the upper facial third volume than the normal reference. Frontal bossing was also found in the presented results. These skeletal findings correlate with the overlying soft tissue features found in this study.

The zygoma and cheeks were evaluated comprehensively in this study. These regions have no anatomically discrete landmarks; therefore, they are difficult to analyze comprehensively in traditional anthropometric or cephalometric studies. Many studies on HED have described the midfacial traits, but it's unclear whether the development of the zygomatic bone is affected. The present study's current results demonstrate recession in the zygomatic region, suggesting that the development of the zygoma, derived from the ectomesenchyme, is affected by this congenital disorder. This finding is supported by a recent study using cone-beam computed tomography to evaluate the zygomatic features of ED,[24] which suggested that the development of zygomatic thickness and length in ED were insufficient.

Cheeks are important for facial esthetics due to high visibility. The sunken cheeks were analyzed quantitatively for the first time in this study. The immediate change in the cheek fully emphasizes the importance of dentures in restoring facial support. Meanwhile, a consequent change in contouring of the zygomatic soft tissue was present. The finding of the improved contours following denture placement in the mid-face needs to confirmed by enlarging sample size in order to verify its statistical significance. These findings will be important in the identification and management of patients.

Depression of the soft tissue on the perinasal area, nasal bridge, and collapsed nasal alar were also found in this study. These concavities showed no change after treatment. The results could be explained by the abnormal development of the nose and perinasal region derived from the ectomesenchyme. Dellavia et al. showed that HED children had a reduced growth of the nose throughout childhood, with no catch-up growth during adolescence.[16] Therefore, additional rhinoplasty may be necessary to improve facial esthetics.

The deviation of lips from the controls was evident both in the upper and lower lip. Compared with normal controls, the everted lower lip was relieved after denture treatment whereas the upper lip contour was still straight. These results suggest that the main reason for abnormality in the lower lip is over closure caused by oligodontia and abnormal growth leading to the protuberance of the upper lip. Pavla et al. reported that the protuberance of the upper lip was related to the shallow contour of the maxilla and short nasal structure.[25]

Due to dysmorphic craniofacial features and defects in the stomatognathic system, HED patients often require prosthetic treatment. Poor growth of the facial skeleton and dental and functional compensation caused by tooth agenesis are correlated with this typical dentofacial pattern in HED.[6,12,16,26] The compromised appearance makes patients more likely to be aware of their differences from healthy peers, causing impaired psychosocial functioning.[27] To minimize orofacial impairment concerning chewing function, speech, and esthetics, the first dentures should be performed before school enrollment. Removable dentures have been recommended to be initially placed at a minimum of two years of age.[8] Dental therapy of HED children is a long-term and active process that requires periodic recall and making adjustments due to the ongoing jaw growth.

Dentures help to replace the missing teeth and support facial musculature, restoring the facial fullness. This study uses an objective, holistic method to evaluate the complete facial form of Chinese male HED children before and after occlusion reconstruction. Posttreatment facial changes provide a better understanding of the dentures' role in improving facial appearance. The occlusal vertical dimension and centric relationship in the mandibular rest position were rebuilt. Chin retruded after denture placement, caused by a clockwise mandibular movement. This can help position the mandibular condylar head correctly within articular fossa, which creates a conducive environment for facial growth.[2]

This study evaluated facial morphology using 3-D imaging and morphometric analysis. 3-D facial surface scanning is an important noninvasive tool to investigate external features and the underlying skeletal pattern. The authors applied spatially dense geometric morphometrics and multivariate statistics to precisely quantify shape and size variation in facial form. The spatially dense landmarking is fully automated; hence, it has high repeatability. It allows monitoring the location, magnitude, and direction of changes over the whole face in a more detailed and accurate way than past 3-D morphometric analyses.[20] This is useful to record subtle changes in facial features that are difficult to capture by linear distances or angle measurements in cephalometric studies.

There are some limitations in this study. First, the sample size is small; HED is a rare syndrome, and only 12 male patients were recruited. Some clinically relevant treatment effects might not be detected and sex differences in HED patients could not be investigated. Another limitation is that facial changes of HED children were evaluated immediately after prosthetic treatment. Understanding the long-term effects of prosthetic treatment on the face and the facial growth trajectory is important. Future work should employ larger samples of males and females and long-term follow-up of patients to investigate these issues.

Conclusions

Based on this study's results, the following conclusions can be made:

1. Hypohidrotic ectodermal dysplasia patients have a more prominent forehead, depressed nasal bridge and alar collapse, depressed zygomatic zone, flat cheeks, protuberant lips, and a more protruding chin. They present with a more concave facial profile, as seen in elderly edentulous people.
2. The contours of the cheeks, lips, zygomatic zone, and chin were improved by denture placement for the HED children. However, compared with the controls, differences after denture placement exist in the patients' perinasal and submental region.
3. Early denture restoration is recommended, as this can improve the facial appearance of the patients.

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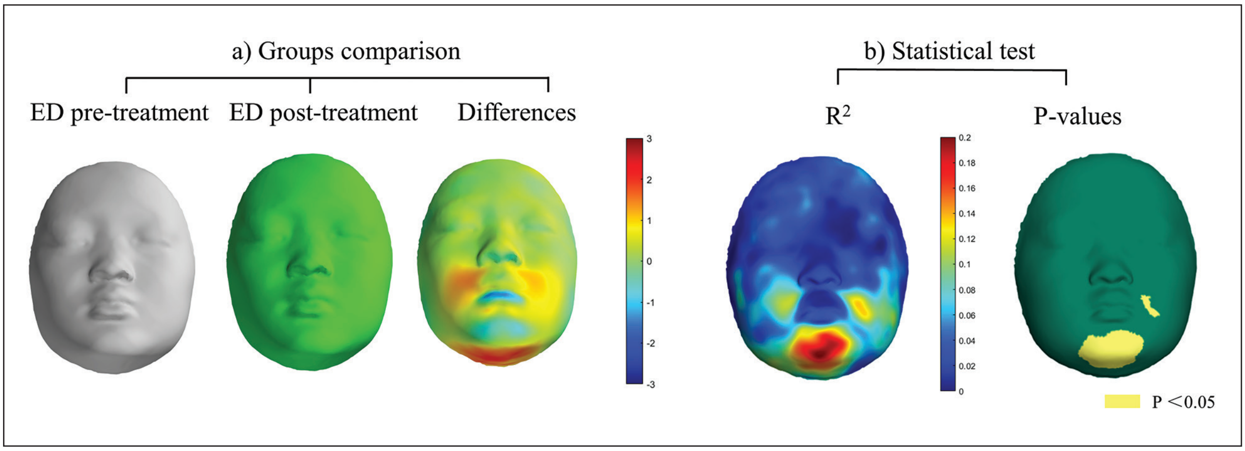
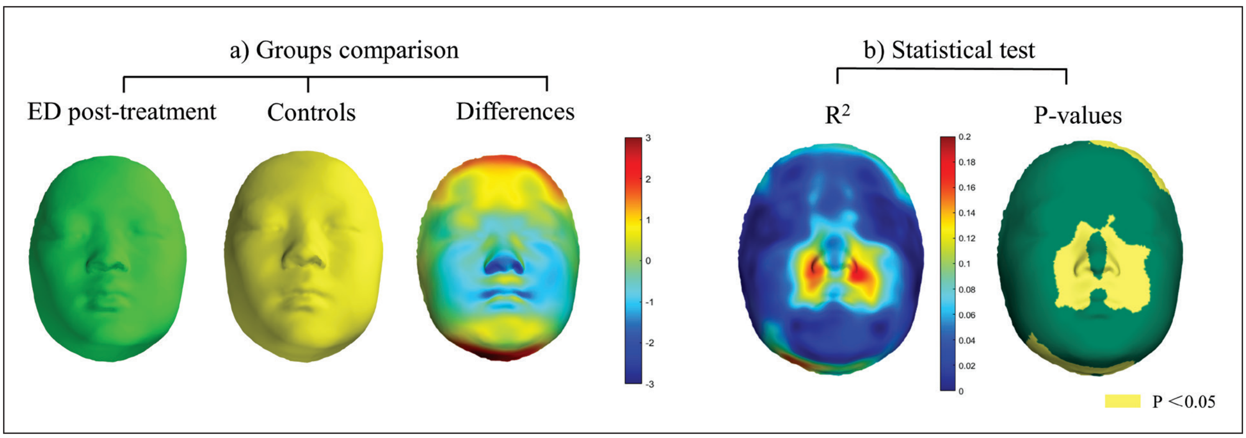
Supplemental Electronic Data

Supplemental Figures 1–2



sFigure 1. (a) Pre- and posttreatment changes of hypohidrotic ectodermal dysplasia patients in facial morphology. Red equals outward displacement; dark blue equals inward displacement. The cheeks and chin become more prominent. (b) R^2 indicates proportion of the total variance in facial morphology that can be explained by group membership. Red equals strongest effect; dark blue equals no effect. The strongest effects are localized in the cheeks and chin region. However, only the changes in the chin are statistically significant (P<0.05), as indicated in yellow.



sFigure 2. (a) Visualization of differences in facial morphology between the hypohidrotic ectodermal dysplasia posttreatment average face and the average face of controls. Red equals outward displacement; dark blue equals inward displacement. A reduced discrepancy is found in the forehead, zygomatic, cheeks, lower lip, and chin region compared to before treatment. (b) R^2 indicates proportion of the total variance in facial morphology that can be explained by group membership. Red equals strongest effect; dark blue equals no effect. The strongest effects are in the area around the nasal wing and submental region. The statistical differences are found around the perinasal area and submental region. Statistically significant areas (P<0.05) are indicated in yellow.