Grenze International Journal of Engineering and Technology, Jan Issue

Deep Learning based Identification of Genetic Syndromes using Facial Images

Shahid Ul Islam Dar[1], Manoj Kumar Gupta[2] and Deo Prakash[3]
[1-3]School of Computer Science and Engineering, Shri Mata Vaishno Devi University, Katra, India
Email: darshahidulislam357@gmail.com, {manoj.gupta, deoprakash}@smvdu.ac.in

Abstract*— A disease that affects a small number of people is termed as a rare disease. Around 4% of the total global population is afflicted with the rare diseases. Even if the symptoms don't manifest right away, the majority of uncommon diseases have a hereditary foundation and are therefore present for the entirety of the person's life. Genetic analysis, the ability to diagnose diseases is continually evolving, and testing is becoming more and more necessary. When sending patients to clinical genetics facilities, however, care must be taken due to the restricted resources, particularly the availability of trained clinical geneticists. Around 30–40% of genetic illnesses are linked to dysmorphic traits, which are unique face characteristics. Recent studies demonstrated the capacity of facial recognition technology to recognize genetic diseases. In this study, we evaluated how well deep learning face recognition model-based classifiers performed in identifying dysmorphic characteristics. Using facial photos and deep convolutional neural networks, this project enhances the early detection of uncommon craniofacial genetic syndromes including Down syndrome, Progeria, Apert and Williams's syndrome. For the treatment of associated medical difficulties and health issues, early diagnosis of rare facial genetic syndromes is essential. According to studies, the existing screening procedures are insufficient, and in many cases, the disease is not discovered until a few years after the kid is born. We evaluated two classification problems, the first being a binary classification problem (Disease vs. Controls) and the second being a multi-class classification problem (5 genetic disorders vs. controls). The five genetic syndromes we are working on are: Down syndrome, Apert syndrome, Progeria Syndrome, Fragile syndrome, and Williams's syndrome. We tried different methods for solving this problem and the best results we achieved were using the VGG-16 inspired CNN. We reached a high level of accuracy by using our dataset with 5 categories to fine-tune the VGG-16 model, with a peak accuracy of 92 percent and an F1-Score of 0.93.With a maximum accuracy of 92 percent and an F1-Score of 0.93, we successfully improved the VGG-16 model using our dataset with 5 categories.

***Index Terms*— Genetic Syndrome, Health Diagnosis, CNN, Deep learning, Facial Genetics.**

I. INTRODUCTION

Genetic disorders can arise when there is a mutation in your genes, which is a harmful change also known as a pathogenic variant, or when the amount of genetic material is incorrect. The genes are made up of DNA (deoxyribonucleic acid), which contains instructions for cellular functions and the distinctive traits of each individual. We receive 50% of our genes from each of our biological parents, and it is feasible to acquire a genetic mutation from either one or both of them. Changes or mutations in genes can occur due to problems with DNA.

Grenze ID: 01.GIJET.10.1.388

The risk of having a genetic disorder may increase if these changes occur. While some genetic disorders present symptoms from birth, others may develop gradually over time.

More than 30 million people in Europe alone suffer from rare diseases, according to [1], there are over 8,000 different types of rare diseases that have a population frequency of less than 1 in 2,000. These disorders have a genetic basis in more than 72% of cases. More than 22,000 genes are encoded by the human genome, and nearly 7500 of these genes have been connected to human diseases [2]. Next-generation sequencing (NGS) technology has significantly increased the diagnostic potential of genetic testing. This approach significantly improves on targeted single gene sequencing by allowing the examination of thousands of genes in one single experiment. Despite the benefits of these technologies, such as the vast amount of data produced and the extensive genetic variability analyzed, their analytical capabilities are limited. The clinical assesment of the patient continues to serve as the foundation for an accurate interpretation of the sequencing data.

Genetic illnesses can affect any part of the human body, including any organ or system. According to [3], between 30 and 40 percent of these diseases are linked to distinctive face traits known as dysmorphic features. Atypical embryological development frequently leads to the dysmorphic traits. For instance, in the case of craniosynostosis, genetic abnormalities cause the early fusion of cranial sutures altering the appearance of the facial skeleton and the form of the skull. Genetic diseases can have other symptoms in addition to dysmorphic features. The diagnostic procedure, severity of the disease, and the disease management are all significantly impacted by other symptoms of genetic abnormalities, such as autism, organ anomalies, and intellectual disability. Genetic counseling's assessment of dysmorphic characteristics is a crucial component, but it requires extensive knowledge and is a highly individualised approach.

In the clinic, doctors typically must distinguish between patients with Genetic syndromes and healthy individuals. In this project, we conducted multiple experiments in this project to examine if computer-assisted facial analysis methods could detect genetic syndromes with dysmorphic features. Consequently, we developed a technique utilizing deep convolutional neural networks to detect individuals with genetic syndromes by analyzing their facial images. This method involved solving a multi-class classification problem by distinguishing individuals with various genetic syndromes from healthy individuals. Picture enhancement, facial detection, facial cropping, and image scaling are the four main phases in the preprocessing of images.

To detect the five syndromes, we fine-tuned the genetic syndrome identification network using transfer learning. Precision, recall, specificity, and F1 score were among the metrics utilized to assess performance. Our approach has significant potential for aiding in the remote identification of genetic disorders using complete automation, making it suitable for use in precision medicine. It provides a rapid, precise, and fully automated clinical tool to identify five distinct forms of rare genetic syndromes.

II. Background And Related Work

Over 30 years have been spent researching the use of computer vision for facial genetic disorder detection. These methods required a significant amount of manual data entry and analysis. Fully connected multi-layer perceptron were employed in one of the earliest neural network applications for the detection of genetic disorders [4]. The grayscale images were manually adjusted, including rotation, scaling, and cropping, to achieve a final size of 55 by 72 pixels. Using an output layer, binary classification between 10 photographs of dysmorphic faces and 21 images of healthy controls was completed with an accuracy rate of 95%. The flattened image (3,960 pixels) was passed through a hidden layer of 2–10 neurons. Using manually annotated landmarks on faces, which ranged in number from 32 [6] to 48 [7] landmarks, it has been possible to measure the geometric properties of the face and extract local textural information.

Gray scale image patches surrounding these landmarks were described using Gabor wavelets [8] of various scales and orientations [6]. To also capture geometric information, [7] looked into the joint use of wavelets around landmarks and their standardized coordinates. Together, frontal and profile face photos underwent this analysis. [5] used the angles between vertices and pairwise distances between landmarks of the 48 manually placed landmarks of the Delaunay triangulation to describe the geometry of syndrome faces. 205 images of 14 syndromes [7], 200 frontal and profile images of 14 syndromes [6], and 55 images of 5 syndromes [6] were all part of relatively small datasets that were collected under controlled lighting and pose conditions with uniform [5]. Each patient was represented by a single image.

It has also been investigated how three-dimensional (3D) imagery can be used to study genetic dysmorphism. Photogrammetric face scanners that capture a depth point-cloud and 2D pictures of a subject are used to gather these images. These scanners are typically large and require specialized operation. Photogrammetric face scanners were used by [9] to record up to 20,000 automatically measured 3D points on the faces of 379 people with one of

four syndromes and 317 healthy controls. 21 3D landmarks were manually added to these to help create a dense surface model (DSM). Classification accuracy for these DSMs for syndromes and control images reached up to 98% using pairwise discriminations. In the subsequent study, 55 people with disorders were photographed with 25,000 automatically measured 3D points on their faces by [10]. 24 3D landmarks were manually added to these to create DSMs, as in [9]. In a more recent work, [11] created face signature heat maps that depict the expansion and contraction in relation to the reference average using 200,000-point clouds and 12 manually annotated landmarks for alignment. Averages for syndrome subsets were also created and contrasted to control averages that were age and sex-matched. Following registration against a predetermined facial template, these were described to obtain 10,000 automatically placed quasi-landmarks. Principal component analysis was used by [11] to create a face space using the quasi landmarks (PCA). [12] automated the placement of over 7,000 quasi-landmarks on the face using techniques like those used by [11]. After that, they investigated the impact of 22q11.2 Deletion syndrome on facial morphology using partial least squares regression. Additionally, [12] produced 3D average faces that demonstrate how the phenotype differs from the average for healthy control.

The manual nature of the techniques in sections 2.1.1 restricts the scope of their use. This is because specified cameras must be used to capture images in identical lighting and pose conditions, and a professional must manually annotate each image. Affordably priced and widely accessible 2D digital cameras are now available. Computer hardware advancements also make computer vision algorithms simpler to train and use. This prompted researchers to study automated facial analysis techniques from common photos that do not require manual annotation.

Automatic annotation of facial landmarks on the face has been achieved using the Constrained Local Model (CLM) [22] and Active Appearance Model (AAM) [13]. Both techniques use a global template model and local landmark classifiers to limit the relative positions of landmarks.

These were used to extract regional geometrical and texture features as well as automatically annotate 44 facial landmarks [14], [15]. These were used to classify people with disorders using support vector machines from controls of the same gender and age (SVM).

130 automatically detected facial landmarks were used to compute local binary patterns[16], which were then used as features to identify Cornelia de Lange syndrome (CdLS) [17]. To find the locations of the 130 facial landmarks, a chains model [23] was initialized using a wavelet-based face detector [24]. In order to compare CdLS and healthy controls, the extracted local binary patterns close by and the landmarks were employed. The algorithm performed noticeably better than experts' detection rates.

Ref. [18] also looked into data fusion between shape and appearance description. The shape descriptor was used to describe faces by adding up all pairwise distances between the 13 facial landmarks and the 36 automatically placed landmarks (the appearance descriptor). These were combined to train the "Clinical Face Phenotype Space," a discriminant embedding that simulates human facial dysmorphisms. Their research into extrapolating generalization to unknown syndromes outside of the training dataset was a significant contribution to the field. 1,363 facial images from 8 syndromes and 1,515 unharmed controls were used in this study.

Deep feature representations are now being used by researchers for the classification of syndromes as a result of developments in deep neural network transfer learning. When classifying genetic disorders, [19] looked into the use of deep representations that had been trained for unrelated tasks. They used SVMs to classify the features that were extracted using an AlexNet trained on ImageNet. Prior to classification, deep representations were extracted for various facial regions and concatenated. With 98.8% accuracy, 1,126 pictures representing 6 syndromes were collected and identified using this method.

Ref. [20] used transfer learning to train DeepGestalt, another part-based model developed by them [19]. The pre-training of various networks for each face part on a large face recognition dataset [21] was followed by fine-tuning on 26,190 syndromic images. At the inference stage, 215 syndromes were jointly predicted from a test set of 502 images using the outputs from individual face-part networks.

III. Dataset Preparation, Model Construction And Evaluation Metrics

A. Dataset Preparation

There aren't many publicly accessible datasets that include the faces of people with genetic disorders. This is because of the rarity of these disorders and confidentiality reasons. We used the Data which is publicly available on Github [25], [26]. The dataset includes 210 photographs of Williams' syndrome patients, 510 photographs of people with Down syndrome, 122 photographs of people with Fragile X syndrome, and 234 photographs of people with Apert syndrome. The control dataset is made up of the face photos of 2876 healthy people. The dataset is summarized in detail in Table 1. For each class, 80% of the images make up the training data, with the remaining 20% being saved for testing.

TABLE I. DATASET DESCRIPTION

Name of syndrome	No. of images
Apert syndrome [27]	234
Down syndrome [28]	510
Fragile syndrome [29]	122
Progeria syndrome [30]	230
Williams syndrome [31]	210
Control Images	2876

Figure 1. Sample images from dataset

B. Model Training

The following is a list of some of the CNN architectures and models that have been utilized for image-based classification tasks:

- VGG-16
- VGG-19
- Le-Net
- Alex-Net
- GoogleNet
- ResNet
- InceptionNet

The models used in our work are inspired by some of these CNN models like ResNet, VGG-16, VGG-19, and Inception-Net. Only VGG-16 and VGG-19 inspired CNNs were used for binary classification; both models were trained on the training set for 30 iterations with a dropout rate of 0.3 and a learning rate of 0.01. On both the training and test data sets, both models showed good performance. For multi-class classification, we first implemented 6 different single models that are VGG-16, VGG-19, ResNet50, and InceptionNet. During the 30 training epochs for all the models, a learning rate of 0.001 was used. The dropout rate was taken as 0.3 and model check-pointing was done using Val-accuracy. The loss function for our implementation of the Adam optimizer was categorical cross-entropy. Finally, we used an ensemble method which included InceptionNetV3, DenseNet201 and XceptionNet and used the ensemble model for the multi-classification task. This ensemble model underwent 40 iterations of training over the training set of data, with a dropout rate of 0.5 and a learning rate of 0.0001. Only the model with the highest accuracy was saved thanks to the model check-pointing on Val-accuracy. As the loss function, categorical cross-entropy was employed.

IV. Results And Conclusion

A. Results on Binary Classification

We first developed the VGG-16-inspired CNN and then utilised VGG-19 to categorise the facial pictures into only two categories (disease vs. controls) for binary classification. We trained both the models for 20 epochs with model check-pointing over Val-accuracy for the binary classification over the augmented dataset. Adam optimizer was applied with a batch size of 128 and a learning rate of 0.01. The classification accuracy of the VGG-16 model was 99.7 over the training data and 98.1 over the test data. The results are described in the tables shown below.

B. Binary Classification using VGG-16

The 554 facial images were classified accurately as diseased and 590 facial images were classified accurately as healthy by our model.

Table II. Classification Report For Binary Classification Using VGG-16

Type	Precision	Recall	F1-Score	Support
Disorder	0.98	0.98	0.98	566
Normal	0.98	0.98	0.98	600
Average	98.1			

C. Binary Classification using VGG-19

The 554 facial images were classified accurately as diseased and 590 facial images were classified accurately as healthy by our model.

Table III. Classification Report For Binary Classification Using VGG-19

Type	Precision	Recall	F1-Score	Support
Disorder	0.99	0.97	0.98	566
Normal	0.97	0.99	0.98	600
Average	97.9			

D. Results on Multi-Class Classification

For multi-class classification i.e., classifying the facial images into five different classes (Apert, Down, Fragile, Progeria, Williams), we implemented different pre-trained models like the VGG-16 inspired CNN, VGG-19, ResNet50V2, InceptionNetV3, and finally we tried some ensemble models as well.

Multi-Class Classification using VGG-16: We trained the model for 30 epochs with model check-pointing over Val-accuracy for the multi-class classification over the augmented dataset. We utilized a learning rate of 0.0001 and a batch size of 256 with the Adam optimizer. Over training data and test data, the model's classification accuracy was 99.9 and 92.9, respectively. The 157 facial images were classified accurately as patients with Apert syndrome, 163 with Down's syndrome, 152 with Fragile syndrome, 183 with Progeria syndrome and 161 with Williams's syndrome.

Table IV. Classification Report For Multi-Class Classification Using VGG-16

Type	Precision	Recall	F1-Score	Support
Apert	0.92	0.91	0.92	173
Down	0.89	0.92	0.91	177
Fragile	0.94	0.87	0.91	174
Progeria	0.94	0.98	0.96	186
Williams	0.95	0.96	0.95	168
Average	92.9			

E. Multi-Class Classification using VGG-19

We trained the model for 30 epochs with model check-pointing over Val-Accuracy for the multi-class classification over the augmented dataset. We utilized a learning rate of 0.0001 and a batch size of 256 with the Adam optimizer. Patients with Apert syndrome, 162 Down's syndrome, 153 Fragile syndrome, 184 Progeria syndrome, and 159 Williams syndrome were correctly identified from 151 face photos.

TABLE V. CLASSIFICATION REPORT FOR MULTI-CLASS CLASSIFICATION USING VGG-19

Type	Precision	Recall	F1-Score	Support
Apert	0.90	0.87	0.89	173
Down	0.87	0.92	0.89	177
Fragile	0.95	0.88	0.91	174
Progeria	0.94	0.99	0.96	186
Williams	0.95	0.95	0.95	168
Accuracy	92.14			

F. Multi-Class Classification using ResNet50V2

We trained the model for 30 epochs with model check-pointing over Val-accuracy for the multi-class classification over the augmented dataset. We utilized a learning rate of 0.0001 and a batch size of 256 with the Adam optimizer. Over the training data and test data, the model's classification accuracy was 99.9 and 91.6, respectively. 157 samples of Apert syndrome, 166 of Down's syndrome, 145 of Fragile syndrome, 177 of Progeria syndrome and 160 of Williams's syndrome were accurately predicted by the ResNet50V2 model.

TABLE VI. CLASSIFICATION REPORT FOR MULTI-CLASS CLASSIFICATION USING RESNETV2

Type	Precision	Recall	F1-Score	Support
Apert	0.92	0.91	0.91	173
Down	0.84	0.94	0.89	177
Fragile	0.95	0.83	0.89	174
Progeria	0.97	0.95	0.96	186
Williams	0.91	0.95	0.93	168
Accuracy	91.6			

G. Multi-Class Classification using InceptionNetV3

We trained the model for 30 epochs with model check-pointing over Val-accuracy for the multi-class classification over the augmented dataset. We utilized a learning rate of 0.0001 and a batch size of 256 with the Adam optimizer. The model achieved the classification accuracy of 97.8 over the training data and 85.7 over the test data. 139 samples of Apert syndrome, 137 of Down's syndrome, 154 of Fragile syndrome, 179 of Progeria syndrome and 144 of Williams syndrome were accurately predicted by the InceptionNetV3 model.

TABLE VII. CLASSIFICATION REPORT FOR MULTI-CLASS CLASSIFICATION USING INCEPTIONNETV3

Type	Precision	Recall	F1-Score	Support
Apert	0.84	0.80	0.82	173
Down	0.81	0.77	0.79	177
Fragile	0.84	0.89	0.86	174
Progeria	0.90	0.96	0.93	186
Williams	0.91	0.86	0.88	168
Accuracy	85.7			

H. Multi-Class Classification using Ensemble Model

Ensemble technique is a machine learning technique in which we combine different base models to produce a more accurate predictive model. There are different ways to implement ensemble model like stacking, averaging etc., we used averaging technique and combined three different models (InceptionNetV3, DenseNet201, XceptionNet) and came up with an ensemble model. We trained the ensemble model for 40 epochs with model check-pointing over Val-accuracy for the multi-class classification over the augmented dataset. We utilized a learning rate of 0.0001 and a batch size of 256 with the Adam optimizer. The model achieved the classification accuracy of 92.7 over the training data and 91.5 over the test data. 133 samples of Apert syndrome, 141 of Down's syndrome, 125 of Fragile syndrome, 180 of Progeria syndrome and 149 of Williams syndrome were accurately predicted by the InceptionResNetV2 model.

TABLE VIII. CLASSIFICATION REPORT FOR MULTI-CLASS CLASSIFICATION USING ENSEMBLE MODEL

Type	Precision	Recall	F1-Score	Support
Apert	0.87	0.95	0.91	173
Down	0.88	0.93	0.91	177
Fragile	0.95	0.82	0.88	174
Progeria	0.93	0.99	0.96	186
Williams	0.97	0.88	0.92	168
Accuracy	91.5			

I. Summary of Results

The results shown below are obtained by fine-tuning the model parameters. This table, which only shows the results of multi-class classification in each trial, summarizes the models we employed in this investigation.

TABLE IX. SUMMARY OF RESULTS

Model	Type	Precision	Recall	F1-Score	Accuracy
VGG-16	0 (Apert)	0.92	0.91	0.92	92.9
	1 (Down)	0.89	0.92	0.91	
	2 (Fragile)	0.94	0.87	0.91	
	3 (Progeria)	0.94	0.98	0.96	
	4 (Williams)	0.95	0.96	0.95	
Weighted Average		0.93	0.93	0.93	
VGG-19	0 (Apert)	0.90	0.87	0.89	92.1
	1 (Down)	0.87	0.92	0.89	
	2 (Fragile)	0.95	0.88	0.91	
	3 (Progeria)	0.94	0.99	0.96	
	4 (Williams)	0.95	0.95	0.95	
Weighted Average		0.92	0.92	0.92	

Model	Type	Precision	Recall	F1-Score	Accuracy
ResNetV2	0 (Apert)	0.92	0.91	0.92	91.6
	1 (Down)	0.84	0.94	0.89	
	2 (Fragile)	0.95	0.83	0.89	
	3 (Progeria)	0.97	0.95	0.96	

	4 (Williams)	0.91	0.95	0.93	
Weighted Average		0.92	0.92	0.92	
InceptionNetV3	0 (Apert)	0.84	0.80	0.82	85.7
	1 (Down)	0.81	0.77	0.79	
	2 (Fragile)	0.84	0.89	0.86	
	3 (Progeria)	0.90	0.96	0.93	
	4 (Williams)	0.91	0.86	0.88	
Weighted Average		0.86	0.86	0.86	
Ensemble Model	0 (Apert)	0.87	0.95	0.91	91.5
	1 (Down)	0.88	0.93	0.91	
	2 (Fragile)	0.95	0.82	0.88	
	3 (Progeria)	0.93	0.99	0.96	
	4 (Williams)	0.97	0.88	0.92	
Weighted Average		0.92	0.92	0.91	

This table shows that all the models we used for this work gave satisfactory results, but VGG-16, VGG-19 and ensemble models performed better than the rest of them. The greatest result was provided by VGG-16, which produced an accuracy of 92.9 percent on the test data. Using ensemble models, we were able to get an accuracy of 91.5 percent. VGG-19 provided an accuracy of 92.1 percent.

V. Conclusion And Future Scope

In the present study, we implemented several Deep learning models that are VGG-16, VGG-19, ResNet50V2, and InceptionNetV3, and ensemble models for the multi-class classification. For Binary classification, we used only VGG-16 AND VGG-19 inspired networks. The dataset we used for this work is an amalgamation of data taken from various sources. The model performances were evaluated using Accuracy, Recall and Precision. We showed that we can produce very accurate results by using a minimal number of photos, pre-trained weights, and then fine-tuning the model parameters. We also proposed an ensemble model of three different models (InceptionNet, DenseNet201 and XceptionNet) which performed better than the single models and achieved an accuracy of 92%. Convolutional Neural Networks have a tremendous potential to support the automatic identification of various rare genetic diseases using facial image data, and can be used in early diagnosis and prevention of disease progression, according to the results we obtained using various models and techniques.

The main problem we faced in this work was the data scarcity problem, we could not get access to a large dataset and in fact a large dataset for this problem is not available due to certain reasons. So, in future we can also expect that the problem of unavailability of data is solved. In this study, we also proposed a new light-weight model for real-world scenarios. This model with only 0.9M parameters achieved an accuracy of 84% on multi-class problem even on a very small dataset. In the future, this model can be applied to low-resource devices with a significantly larger dataset and improved quantization and trimming techniques.

Only five rare genetic syndromes were taken into consideration in this study, despite the fact that thousands of genetic syndromes have been identified to date, and the number is growing over time. So, if enough data is available for other syndromes as well, then these methods can be used on those syndromes also. Future research can look into further genetic disorders that alter the facial features.

References

[1] Rodwell, C.; Aymé, S. (Eds.) 2014 Report on the State of the Art of Rare Disease Activities in Europe. July 2014.

[2] S. Nguengang Wakap et al., “Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database,” European Journal of Human Genetics 2019 28:2, vol. 28, no. 2, pp. 165–173, Sep. 2019, doi: 10.1038/s41431-019-0508-0.

[3] W. Reardon and D. Donnai, “Dysmorphology demystified,” Arch Dis Child Fetal Neonatal Ed, vol. 92, no. 3, p. F225, May 2007, doi: 10.1136/ADC.2006.110619.

[4] R. Herpers, H. Rodax, and G. Sommer, “A Neural Network Identifies Faces with Morphological Syndromes,” pp. 481–485, 1993, doi: 10.3233/978-1-60750-854-0-481.
[5] B. Balliu, R. P. Würtz, B. Horsthemke, D. Wieczorek, and S. Böhringer, “Classification and Visualization Based on Derived Image Features: Application to Genetic Syndromes,” PLoS One, vol. 9, no. 11, p. e109033, Nov. 2014, doi: 10.1371/JOURNAL.PONE.0109033.
[6] H. S. Loos, D. Wieczorek, R. P. Würtz, C. von der Malsburg, and B. Horsthemke, “Computer-based recognition of dysmorphic faces,” European Journal of Human Genetics 2003 11:8, vol. 11, no. 8, pp. 555–560, Jul. 2003, doi: 10.1038/sj.ejhg.5200997.
[7] T. Vollmar et al., “Impact of geometry and viewing angle on classification accuracy of 2D based analysis of dysmorphic faces,” Eur J Med Genet, vol. 51, no. 1, pp. 44–53, Jan. 2008, doi: 10.1016/J.EJMG.2007.10.002.
[8] T. S. Lee, “Image representation using 2d gabor wavelets,” IEEE Trans Pattern Anal Mach Intell, vol. 18, no. 10, pp. 959–971, 1996, doi: 10.1109/34.541406.
[9] P. Hammond et al., “Discriminating Power of Localized Three-Dimensional Facial Morphology,” Am J Hum Genet, vol. 77, no. 6, p. 999, 2005, doi: 10.1086/498396.
[10] P. Hammond, M. Suttie, R. C. Hennekam, J. Allanson, E. M. Shore, and F. S. Kaplan, “The face signature of fibrodysplasia ossificans progressiva,” Am J Med Genet A, vol. 158A, no. 6, pp. 1368–1380, Jun. 2012, doi: 10.1002/AJMG.A.35346.
[11] S. Kung et al., “Monitoring of Therapy for Mucopolysaccharidosis Type I Using Dysmorphometric Facial Phenotypic Signatures,” JIMD Rep, vol. 22, pp. 99–106, 2015, doi: 10.1007/8904_2015_417.
[12] Lewyllie et al., “A Comprehensive Craniofacial Study of 22q11.2 Deletion Syndrome,” J Dent Res, vol. 96, no. 12, pp. 1386–1391, Nov. 2017, doi: 10.1177/0022034517720630.
[13] T. F. Cootes, G. J. Edwards, and C. J. Taylor, “Active appearance models,” Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), vol. 1407, pp. 484–498, 1998, doi: 10.1007/BFB0054760/COVER.
[14] Q. Zhao et al., “Digital facial dysmorphology for genetic screening: Hierarchical constrained local model using ICA,” Med Image Anal, vol. 18, no. 5, pp. 699–710, Jul. 2014, doi: 10.1016/J.MEDIA.2014.04.002.
[15] P. Kruszka et al., “22q11.2 deletion syndrome in diverse populations,” Am J Med Genet A, vol. 173, no. 4, pp. 879–888, Apr. 2017, doi: 10.1002/AJMG.A.38199.
[16] T. Ahonen, A. Hadid, and M. Pietikäinen, “Face recognition with local binary patterns,” Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), vol. 3021, pp. 469–481, 2004, doi: 10.1007/978-3-540-24670-1_36/COVER.
[17] L. Basel-Vanagaite et al., “Recognition of the Cornelia de Lange syndrome phenotype with facial dysmorphology novel analysis,” Clin Genet, vol. 89, no. 5, pp. 557–563, May 2016, doi: 10.1111/CGE.12716.
[18] Q. Ferry et al., “Diagnostically relevant facial gestalt information from ordinary photos,” Elife, vol. 2014, no. 3, Jun. 2014, doi: 10.7554/ELIFE.02020.001.
[19] P. Shukla, T. Gupta, A. Saini, P. Singh, and R. Balasubramanian, “A deep learning frame-work for recognizing developmental disorders,” Proceedings - 2017 IEEE Winter Conference on Applications of Computer Vision, WACV 2017, pp. 705–714, May 2017, doi: 10.1109/WACV.2017.84.
[20] Y. Gurovich et al., “DeepGestalt - Identifying Rare Genetic Syndromes Using Deep Learning,” Jan. 2018, Accessed: Aug. 13, 2023. [Online]. Available: https://arxiv.org/abs/1801.07637v1
[21] D. Yi, Z. Lei, S. Liao, and S. Z. Li, “Learning Face Representation from Scratch,” Nov. 2014, Accessed: Aug. 13, 2023. [Online]. Available: https://arxiv.org/abs/1411.7923v1
[22] D. Cristinacce and T. Cootes, “Automatic feature localisation with constrained local models,” Pattern Recognit, vol. 41, no. 10, pp. 3054–3067, Oct. 2008, doi: 10.1016/J.PATCOG.2008.01.024.
[23] L. Karlinsky, M. Dinerstein, D. Harari, and S. Ullman, “The chains model for detecting parts by their context,” Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition, pp. 25–32, 2010, doi: 10.1109/CVPR.2010.5540232.
[24] P. Viola and M. J. Jones, “Robust Real-Time Face Detection,” Int J Comput Vis, vol. 57, no. 2, pp. 137–154, May 2004, doi: 10.1023/B:VISI.0000013087.49260.FB/METRICS.
[25] “arjun619/Downs_Syndrome_Detection.” https://github.com/arjun619/Downs_Syndrome_Detection (accessed May 04, 2023).
[26] “taqbi/Genetic-Disorder.” https://github.com/taqbi/Genetic-Disorder (accessed May 04, 2023).
[27] “Apert Syndrome | Boston Children’s Hospital.” https://www.childrenshospital.org/conditions/apert-syndrome (accessed May 08, 2023).
[28] “Down syndrome - Symptoms and causes - Mayo Clinic.” https://www.mayoclinic.org/diseases-conditions/down-syndrome/symptoms-causes/syc-20355977 (accessed May 08, 2023).
[29] “What is Fragile X Syndrome (FXS)? | CDC.” https://www.cdc.gov/ncbddd/fxs/facts.html (accessed May 08, 2023).
[30] “Progeria - Symptoms and causes - Mayo Clinic.” https://www.mayoclinic.org/diseases-conditions/progeria/symptoms-causes/syc-20356038 (accessed May 08, 2023).
[31] “Williams Syndrome, Williams Beuren Syndrome: Causes, Symptoms & Treatment.” https://my.clevelandclinic.org/health/diseases/15174-williams-syndrome (accessed May 08, 2023).