Recognition of Genetic Diseases Based on Combined Feature Extraction from 2D Face Images

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***Abstract*—Screening patients with genetic diseases using automated facial image analysis is an urgent task. A method for recognizing genetic syndromes from a frontal image of a face has been developed and studied. The classification was made to 8 syndromes (Angelman, Apert, Cornelia de Lange, Down, Fragile X, Progeria, Treacher Collins, Williams). Various types of features were investigated: geometric and deep features. For facial points localization, 3D face reconstruction was used (using the Deep3DFaceReconstruction library). Sets of 68 and 35709 (all points of 3D reconstruction) points were investigated. The effect of reducing the dimension of the feature vector on the classification accuracy is also investigated. According to the results of 5-fold cross-validation, the best average recognition accuracy was 92.5 % (combined features, Principal Component Analysis (PCA), Linear Discriminant Analysis (LDA) and logistic regression), which is comparable to the results in similar works.**

I. Introduction

According to the World Health Organization, almost 8 % of the population suffers from genetic diseases, more than 7000 of these diseases are known. Genetic pathology is a significant part in the structure of childhood morbidity, mortality and disability.

Despite the growing importance of molecular genetic methods and increasing their effectiveness in the diagnosis of genetic diseases, the analysis of phenotypic manifestations remains extremely important, because it provides not only the definition of a clinical hypothesis, but also the correct interpretation of laboratory results. The description of the face and head is especially important, since from 30 to 40 % of genetic diseases are accompanied by changes in the anatomical structure of the craniofacial region [1].

After birth, the initial diagnosis is largely based on a visual examination of the child, as those suffering from genetic syndromes have distinctive facial features, and cranial-facial characteristics in this case are informative. Early diagnosis makes it possible to start treatment measures in a timely manner and prevent the development of complications.

Using easily available disease predictors can help screening of the genetic diseases at an early age. A number of studies have shown the possibility of using facial image analysis for such screening.

The task of recognizing genetic syndromes by facial image can be formulated in different ways. The following problem statements are possible.

The task of the binary classification “syndrome/not a syndrome”: the task is to distinguish a person with a certain syndrome from a healthy group or people with other syndromes ([2], [3], [4], [5], [6], [7], [8], [9]).

The task of the binary classification "syndromes/norm": the task is to distinguish a person with any syndrome from a healthy group ([4], [9], [10]).

The task of the multiclass classification “syndrome/several syndromes”: the task is to choose the right syndrome from the set of possible syndromes ([9], [11], [12], [13], [14], [15], [16], [17], [18]).

Works on the multiclass classification of genetic syndromes are given in Table I.

TABLE I. Results review

Ref.	Number of genetic syndromes	Number of images in training set	Evaluation	Accuracy (rank r = 1)
[9]	6	1126	5-fold CV	48 %
[11]	5	55	Leave-One-Out	76 %
[12]	15	92	Leave-One-Out	53 %
[13]	10	147	10-fold CV	75,70 %
[14]	14	202	91 images (test set)	21 %
[15]	216	26190	502 images (test set)	60 % (r = 1), 83.7 % (r = 5), 91 % (r = 10)
[16]	8	1363	Leave-One-Out	93.10 %
[17]	9	1686	4:1 ratio (10 repeats) (training and testing)	90.29 %
[18]	8	1025 (before augmenting)	70:20:10 ratio (training, validation, and testing)	93.10 % (based on confusion matrix)

According to the classification given in [15], feature extraction methods can be divided into the following groups: holistic methods, local features based methods, statistical model based methods, deep convolutional neural network methods.

An example of work using holistic methods for feature extraction is [12], in which PCA-based eigenfaces are used as the global face representation.

Local features based methods involve the analysis of local regions of the face with the subsequent construction of a combined feature vector. Local features can be appearance-based (Local Binary Patterns – LBP, Scale-Invariant Feature Transform – SIFT, Oriented FAST (Features from Accelerated Segment Test) and Rotated BRIEF (Binary Robust Independent Elementary Features) – ORB [17], Gabor wavelets (as in [11], [13], [14]) or geometric (coordinates of points, distances and angles as in [16], [17]).

An example of using statistical model based methods is [16], where the Active Appearance Model (AAM), trained on facial images of patients for more accurate localization of facial points, is used. AAM is also used for visual representation of canonical phenotypes.

Deep convolutional neural network methods are based on the use of pre-trained corresponding neural networks for feature extraction (as in [9], [17]).

The classification methods used are k-nearest neighbors – kNN (in [12], [13] [16], [17]), Support Vector Machines – SVM ([9], [13], [16], [17] , [18]), LDA (used in [13]), logistic regression ([14], [17]), Gaussian naïve Bayes (as in [17]), and neural networks ([15] , [18]).

The performance of machine learning methods depends on the database used for training and testing. In [16], [17] and [18], the same database was used, collected by the authors of [16] from publicly available sources.

In [16], the "Clinical Face Phenotype Space" was constructed. Pixel intensities of patches around the 9 inner facial feature points and normalized pairwise distances between 36 facial feature points are used as features; kNN with a trained metric (Large Margin Nearest Neighbor – LMNN) is used as a classification method. The classification accuracy was 93.1 % when assessed by the first rank for 8 syndromes.

The same set was used in [17] for training, but other images from the Dartmouth Database of Children's Faces [19] were used for the control group. The use of combined features and the application of dimensional reduction methods (deep, geometric and ORB representation + PCA + LDA + Gaussian naïve Bayes) made it possible to achieve an accuracy of 90.29 %.

In [18], using the fine-tuning of the pre-trained model VGGFace (with ResNet50 network architecture), the accuracy of 93.1 % was obtained (based on confusion matrix for 8 syndromes).

Despite the large number of works in this field, the task of finding the best set of features and a method for automatically recognizing possible hereditary syndromes by facial image remains relevant and in demand in medical genetics.

II. Genetic diseases recognition algorithm

A. Genetic diseases recognition algorithm

The steps of the developed genetic diseases recognition algorithm are:

- preprocessing,
- feature extraction,
- dimensionality reduction,
- classification.

B. Preprocessing

Face detection and alignment of facial images was made using the dlib library [20]. The face images have a resolution of 224×224.

C. Feature Extraction

1) Geometric features: The most frequently used set of 68 control points of the face (in particular, in the dlib library) was selected as geometric features. However, the Deep3DFaceReconstruction library [21] based on [22] was used for automatic point detection. This library allows one to get 3D face reconstruction from a single image, consisting of 35709 points, as well as 3D coordinates of a standard set of 68 points and their 2D coordinates on the original image by projecting the model points on the original image. The use of this software solution is justified by the low quality of point detection using the dlib library on face images of patients with genetic syndromes. The use of all 3D reconstruction points allows one to establish phenotypic features that are not reflected in the standard set of points. But the increasing of recognition accuracy for the extended set of points is not clear.

The Deep3DFaceReconstruction library requires preliminary marking of 5 points on the face (eye centers, tip of the nose, corners of the mouth). The coordinates of these 5 points are determined using the MTCNN library [23], based on [24]. Moreover, the localization of these points is made on an already aligned face image using dlib. This approach (not the direct use of the coordinates returned by dlib) allows one to better determine the coordinates of the points and make a more accurate 3D face reconstruction.

An example of a face image, a set of 68 face points and 3D face reconstruction are shown in Fig. 1.

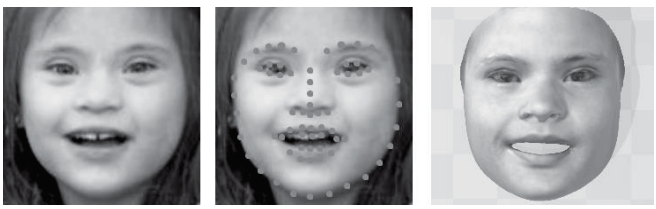

Fig. 1. Geometric features (face image, set of 68 face points and 3D face reconstruction)

2) Deep features: Pre-trained neural network models were used to extract features (deep features). A face image is the input on the neural network, and the output values of the last layers are taken as a feature vector.

There are several neural network models trained on large samples of facial images that are applicable for this task. These include the VGGFace [25], ResNet50 [26], and its modification – SENet50 [27] models.

VGGFace is a convolutional neural network based on the VGG16 architecture, which uses the triplet loss function and is pre-trained on more than 2.6 million facial images of 2622 people. VGGFace network architecture is shown in Figure 2.

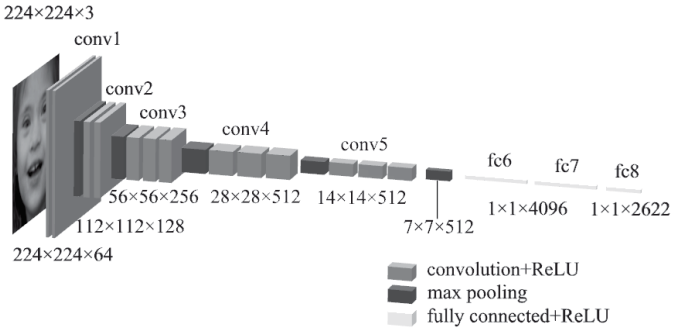

Fig. 2. VGGFace network architecture

VGGFace model uses convolutional layers with 3×3 kernel size. Fig. 2 shows the dimensions of the layers (height, width, depth). Convolutional layers are accompanied by ReLU rectification units.

The last 3 layers are fully connected (FC). The output dimension of the first two FC layers ("fc6" and "fc7") is 4096 each, of the last FC layer ("fc8") – 2622.

ResNet50 is a convolutional neural network based on the "residual network" architecture. This network is based on VGG networks, but with fewer filters and less complexity. A key feature of this network is the use of shortcut connections between blocks that turn the network into a residual version of the network. For the task of analyzing facial images, the ResNet50 model was trained on the basis of VGGface2, which contains 3.331 million images of 9321 people.

A comparison of the VGGFace and ResNet50 models was made in [28]. The VGGFace model surpassed the ResNet50 model in the classification accuracy of face images by gender (94.8 % versus 89.01 %) and ethnic group (90.1 % and 80.05 %). Therefore, the VGGFace model was preferred.

In the VGGFace model, it is possible to select different output layers ("fc6", "fc7", and "fc8") as a feature vector. In [29], the accuracy of image classification was compared using different output layers as a feature vector. Two models were investigated: VGG16 and VGG19 (the architecture is the same, but the network is trained not on face images, but on images of different classes of ImageNet database). The best results were obtained using the "fc6" layer.

Based on the studies described above, the VGGFace model was chosen, the output values of the "fc6" layer are used as deep features.

D. Dimensionality Reduction

Since the resulting feature vectors have a large dimension (for example, for deep features – 4096, for all points of 3D face reconstruction – 107127), it is advisable to use dimensionality reduction methods – PCA and LDA.

An independent sequential application of PCA and LDA to geometric and deep features was used, followed by combining the features into a single feature vector.

The number of PCA components was selected to maintain 95 % and 99 % variation.

E. Classification

The classification was applied in the feature space obtained after dimensionality reduction. The following classification methods were used: kNN, linear and RBF SVM, random forest, LDA, logistic regression, Gaussian naïve Bayes.

III. Dataset

The database of images of persons was provided by the authors of [16]. The database contains images of the faces of patients with 12 syndromes, of which 8 syndromes were selected for the study (Angelman, Apert, Cornelia de Lange, Down, Fragile X, Progeria, Treacher Collins, Williams). Examples of images from the database are shown in Fig. 3.

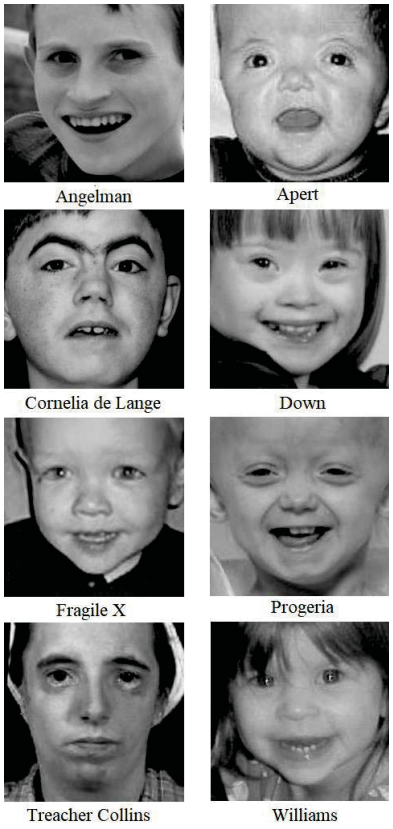

Fig. 3. Examples of images from the database

Images are collected from open sources. This database is characterized by great variability in parameters (lighting conditions, facial expressions, head pose, resolution, background, age, gender, and ethnicity). The number of images for each syndrome is given in Table II. The number of images used in the study is less than in the original database, since a set of images for which faces were not detected or there was an

error during alignment was excluded (the initial task was to avoid manually marking points, so it was decided not to include these images in the sample instead of manually adjusting the position of the points).

TABLE II. IMAGE DATABASE

Syndromes	Number of images
Angelman	204
Apert	194
CDL	246
Down	190
Fragile X	158
Progeria	142
Treacher Collins	101
Williams	227
Total	1462

IV. EXPERIMENTAL RESULTS

The test results (5-fold cross-validation) of the developed algorithm using different classification methods are shown in Table III. For geometric features high classification accuracy was obtained using LDA, logistic regression, linear and RBF SVM (SVM is excluded from further research due to long training and worse accuracy compared to logistic regression). It should be noted that the best recognition accuracy was shown by the LDA (87.7 % for 2D, 90.1 % for 3D). Using an additional third coordinate, reconstructed using 3D face reconstruction from a single image, increases recognition accuracy for all types of classifiers, which indicates the appropriateness of using this approach.

TABLE III. CLASSIFICATION RESULTS FOR DIFFERENT FEATURE SETS

Classification	2D points (68)	3D points (68)	Deep features (VGGFace)
kNN	0.382	0.637	0.729
Linear SVM	0.813	0.825	0.870
RBF SVM	0.813	0.826	0.873
Random Forest	0.520	0.710	0.832
LDA	0.877	0.901	0.778
Logistic Regression	0.827	0.847	0.880
Gaussian Naïve Bayes	0.320	0.598	0.630

In Table III the test results of the developed algorithm using deep features and different classification methods are also shown. Deep features are very informative (the best classification accuracy is 88 % for logical regression). Comparing the results for each of the classification methods for deep features with the results for 2D and 3D points shows that deep features are superior to geometric features in the classification accuracy in general. The only exception is the LDA (87.7 % and 90.1 % for 2D and 3D points versus 77.8 % for deep features). The accuracy (90.1%) for 68 3D points and LDA as a classifier is one of the best in the work, although the feature vector has a small dimension (3*68) and the LDA with many assumptions is used.

In the next series of experiments PCA for dimensionality reduction was used. The dimensions of the feature vectors and the number of principal components while saving a different level of variation are shown in Table IV.

TABLE IV. FEATURE VECTOR DIMENSIONS

Features	Initial Dimension	Maintained variation for PCA, %	PCs
68 2D points	136	95 %	7
		99 %	14
68 3D points	204	95 %	13
		99 %	27
All points	107127	95 %	16
		99 %	33
Deep features	4096	95 %	508
		99 %	938

The test results (5-fold cross-validation) of the developed algorithm using different geometric features, classification methods and PCA (95 %, 99 %) are shown in Table V. The use of PCA has led to a decrease in the classification accuracy (even while saving 99 % variation).

TABLE V. CLASSIFICATION RESULTS WITH DIMENSIONALITY REDUCTION BY PCA ONLY

Classificator	Maintained variation for PCA, %	2D points (68)	3D points (68)	3D points (35709)
kNN	95	0.386	0.646	0.631
	99	0.557	0.705	0.693
Random Forest	95	0.421	0.654	0.687
	99	0.588	0.718	0.749
LDA	95	0.383	0.690	0.747
	99	0.608	0.797	0.834
Logistic Regression	95	0.383	0.689	0.748
	99	0.620	0.789	0.828
Gaussian Naïve Bayes	95	0.386	0.666	0.715
	99	0.575	0.745	0.792

The test results (5-fold cross-validation) of the developed algorithm using different geometric features, classification methods, PCA (95 %, 99 %) and LDA are shown in Table VI. The use of LDA after PCA leads to an increase in accuracy for all classification methods.

TABLE VI. CLASSIFICATION RESULTS WITH DIMENSIONALITY REDUCTION BY SEQUENTIAL APPLICATION OF PCA AND LDA

Classificator	Maintained variation for PCA, %	2D points (68)	3D points (68)	3D points (35709)
kNN	95	0.386	0.665	0.702
	99	0.594	0.778	0.815
Random Forest	95	0.425	0.693	0.727
	99	0.611	0.774	0.814
Logistic Regression	95	0.383	0.691	0.754
	99	0.611	0.792	0.829
Gaussian Naïve Bayes	95	0.396	0.678	0.743
	99	0.608	0.796	0.832

A complete set (35709) of 3D face reconstruction points with PCA and LDA to reduce dimensionality gives a significant increase in classification accuracy (for Gaussian naïve Bayes, PCA (99 %) and LDA accuracies for 2D (68), 3D

(68) and the full set of 3D (35709) points are 60.8 %, 79.6 %, and 83.2 % respectively). However, the use of a full set of points requires the use of dimensionality reduction methods. The best accuracy for a set of all points with PCA (83.4 %) is less than for 68 3D points without PCA (90.1 %). Additional information contained in the full set of points does not give an increase in accuracy, possibly due to dimension reduction.

The test results of the developed algorithm using different classification methods, PCA (95 %, 99 %) and LDA are shown in Table VII. Applying PCA to deep features has different effects for different classification methods. An increase in the classification accuracy occurs only when using the LDA; for other methods, this leads either to noticeable (random forest, kNN, Gaussian naïve Bayes), or insignificant (logistic regression) decrease in the classification accuracy. Moreover, the results for deep features are better for 95 % variation than 99 %, although for geometric features, on the contrary, higher values were achieved at a variation level of 99 %. This may be due to the fact that dimension reduction removes noise from deep features, while for geometric features, using a larger number of main components allows one to save more information, the influence of the noise in this case is less.

TABLE VII. CLASSIFICATION RESULTS WITH DIMENSIONALITY REDUCTION FOR DEEP FEATURES (VGGFACE)

Classificator	Maintained variation for PCA, %	Dimensionality reduction	
		PCA only	PCA+LDA
kNN	95	0.430	0.892
	99	0.328	0.873
Random Forest	95	0.767	0.886
	99	0.739	0.847
LDA	95	0.880	-
	99	0.867	-
Logistic Regression	95	0.880	0.893
	99	0.858	0.872
Gaussian Naïve Bayes	95	0.508	0.880
	99	0.401	0.850

The test results of the developed algorithm using different classification methods, PCA (95 %, 99 %) and LDA are also shown in Table VII. The additional use of LDA leads to improved classification accuracy compared to using a single PCA. The improvement in classification accuracy is also noticeable when compared with the approach without the use of dimensionality reduction methods. For deep features without dimensionality reduction, the best accuracy was 88 % (logistic regression), after dimensionality reduction by PCA (95 %) + LDA, the accuracy for logistic regression became 89.3 %. This result is the best for deep features, which indicates the appropriateness of applying dimensionality reduction techniques.

The test results (5-fold cross-validation) of the developed algorithm using combined features are shown in Table VIII. For all classification methods, with the exception of kNN and Gaussian naïve Bayes, there is an increase in the classification accuracy compared to each type of features used separately. For kNN and Gaussian naïve Bayes, accuracy when using combined features is lower than when using points, but superior to accuracy with deep features.

TABLE VIII. CLASSIFICATION RESULTS WITH DIMENSIONALITY REDUCTION FOR COMBINED FEATURES

Classificator	Maintained variation for PCA, %	Dimensionality reduction	
		PCA only	PCA+LDA
kNN	95	0.466	0.884
	99	0.349	0.886
Random Forest	95	0.804	0.891
	99	0.791	0.868
LDA	95	0.886	-
	99	0.868	-
Logistic Regression	95	0.884	0.891
	99	0.884	0.893
Gaussian Naïve Bayes	95	0.553	0.889
	99	0.466	0.870

The test results (5-fold cross-validation) of the developed algorithm using combined features, PCA (95 %, 99 %) and LDA are also shown in Table VIII. The use of LDA can further improve classification accuracy.

The best results with and without dimension reduction were obtained using the methods, which are shown in Table IX.

A simple set of three-dimensional coordinates of 68 3D points with LDA as a classifier showed the best result (90.1 %) among methods without dimension reduction. This proves the importance and informativeness of geometric features in the recognition of hereditary diseases.

The steps for best method with dimension reduction were selected experimentally, namely, feature sets, number of principal components for PCA, additional use of LDA, and classification method.

TABLE IX. BEST RESULTS

Features	Classification	Dimension Reduction	Accuracy
68 3D points	LDA	-	0.901
Combined: 68 3D points, deep features	Logistic Regression	68 3D points: LDA deep features: PCA (508 PCs) + LDA	0.924
Combined: all 3D points, deep features	Logistic Regression	all points: PCA (110 PCs) + LDA deep features: PCA (508 PCs) + LDA	0.925

The best classification accuracy of 92.5 % is achieved using combined features (deep features and all 3D reconstruction points), subsequent independent dimensionality reduction by PCA and LDA and classification using logistic regression. For 3D points the number of PCs is higher than for 99 % of variance maintaining; for deep features – it equals the number of PCs with 95 % of variance. A similar result (92.4 %) was obtained when using a set of 68 3D points together with deep

features (68 3D points – LDA, deep features – PCA (95 %) and LDA, logistic regression as a classifier).

In [17], an accuracy of 90.29 % was achieved on a similar set using combined features, and the set was expanded with images of a control healthy group (that is, a 9-class problem was solved). However, only using geometric features, the authors managed to achieve a maximum accuracy of 65.82 %, while using the coordinates of points in this study allowed one to achieve an accuracy of more than 80 %.

In [18], the average classification accuracy when using fine tuning and the ResNet50 model on a similar set (some images are excluded from the sample) achieved an accuracy of about 93 % (based on the confusion matrix).

A comparison of our results with the results of [16], [17], [18] allows us to talk about the comparability of the classification accuracy.

VII. Conclusion

The paper compares different features and classifiers for the automatic recognition of genetic syndromes from a 2D face image. Different sets of facial points (68 and 35709 points) and deep features extracted using the VGGFace neural network model were used. It is shown that 3D face reconstruction obtained from a single frontal image allows one to obtain additional features and increase the classification accuracy compared to using of 2D points. The use of combined features can further increase the classification accuracy.

The independent use of geometric and deep features gives approximately the same accuracy. The use of dimensionality reduction methods allows one preserving the classification accuracy with a significant decrease in the dimension of the feature vector. The best classification accuracy of 92.5 % is achieved using combined features (deep features and all 3D reconstruction points), subsequent independent dimensionality reduction using PCA and LDA and classification using logistic regression.

Using a set of coordinates of 68 3D points only and quite simple classifier (LDA) without the dimensional reduction methods allows one to obtain an accuracy of 90.1 %, which indicates the high informativeness of geometric features and the possibility to use classical recognition methods to solve the considered medical problem.

Thus, in the work, different sets of features and methods for automatically recognizing possible hereditary syndromes by facial imagery were investigated, and the prospects for the use of geometric and deep features were shown.

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