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Research Paper

Automatic Detection of Acromegaly From Facial Photographs Using Machine Learning Methods

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ABSTRACT

Background: Automatic early detection of acromegaly is theoretically possible from facial photographs, which can lessen the prevalence and increase the cure probability.
Methods: In this study, several popular machine learning algorithms were used to train a retrospective development dataset consisting of 527 acromegaly patients and 596 normal subjects. We firstly used OpenCV to detect the face bounding rectangle box, and then cropped and resized it to the same pixel dimensions. From the detected faces, locations of facial landmarks which were the potential clinical indicators were extracted. Frontalization was then adopted to synthesize frontal facing views to improve the performance. Several popular machine learning methods including LM, KNN, SVM, RT, CNN, and EM were used to automatically identify acromegaly from the detected facial photographs, extracted facial landmarks, and synthesized frontal faces. The trained models were evaluated using a separate dataset, of which half were diagnosed as acromegaly by growth hormone suppression test.
Results: The best result of our proposed methods showed a PPV of 96%, a NPV of 95%, a sensitivity of 96% and a specificity of 96%.
Conclusions: Artificial intelligence can automatically early detect acromegaly with a high sensitivity and specificity.

1. Introduction

Acromegaly is caused by persistent excessive secretion of growth hormone (GH), usually resulting from somatotroph adenomas. It once has been regarded as one of the rare diseases, whose estimated prevalence is around 0.07‰ in Europe. More recently a higher prevalence of about 130 per million has been suggested by a study in Belgium with more active surveillance for pituitary adenomas (Ribeiro-Oliveira Jr and Barkan, 2012; Melmed and Acromegaly, 1990; Chanson et al., 1989; Reddy et al., 2010). Nevertheless, current prevalence is significantly higher (1‰ in population) (Schneider et al., 2008). As acromegaly course is insidious, often resulting in a delay of 7–10 years in diagnosis after the suspected symptoms and signs onset, few patients seek care due to their appearances' changing (Utiger, 2000; Melmed, 2006). When diagnosed, 75%–80% patients have macroadenomas with some even presenting invasive growth pattern, such as a higher Ki-67 index, expansion and invasiveness (Katznelson et al., 2014). Uncontrolled GH/IGF-1 excess results in increased prevalence and mortality, whereas these could be prevented with the timely and successful disease control, thus early detection of acromegaly is crucial. The variety of disease manifestations might lead patients to refer to the doctors of different specialties (dentist, hand surgeon, ophthalmologist, gynecologist, etc.) that can result in even longer delay of the diagnosis of acromegaly.

Recently, artificial intelligence (AI) increasingly shines brilliantly through the medical area (Hamet and Tremblay, 2017; Obermeyer and Emanuel, 2016; Gencturk et al., 2013). Several peer-review/high-impact-factor journals have published studies using AI helping with assistant diagnosis (Gulshan et al., 2016; Esteva et al., 2017; Kanakasabapathy et al., 2017). Since facial-features of acromegaly are very typical: widening teeth spacing, prognathism, frontal-bone enlargement, nose enlargement, zygomatic-arch prominence, brow ridge and forehead protrusion/prominence, soft tissue swelling (lips, nose,

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ears enlargement) and skin thickening, we herein developed a computational, automatic and handy face-recognition system which may allow doctors or patients to proactively track facial-features changes and detect acromegaly. Using 1123 face photographs, we trained and integrated several machine learning methods including Generalized Linear Models (LM), K-nearest neighbors (KNN), Support Vector Machines (SVM), Forests of randomized trees (RT) and Convolutional Neural Network (CNN) to create an Ensemble Method (EM) for facial detection of acromegaly. Other than the typical facial changes, symptoms and signs of acromegaly also include stimulation of growth of many tissues, such as skin, connective tissue, cartilage, bone, viscera, and many epithelial tissues. The metabolic effects include nitrogen retention, insulin antagonism, and lipolysis. The variety of disease manifestations of acromegaly might lead patients to refer to the doctors of different specialties (dentist, hand surgeon, ophthalmologist, gynecologist, etc.) that can result in even longer delay of the diagnosis of acromegaly. On the other hand, these doctors probably could benefit from algorithms of automatic detection of acromegaly developed by us.

2. Results

2.1. Ensemble Method of LR, KNN, SVM, RT and CNN

The goal of ensemble method was to combine the outcomes of some weak estimators in order to achieve higher classification accuracy as well as better generalizability and robustness. The three most popular methods for combining the predictions from different models were Bagging, Boosting and Voting. Herein, Bagging was used to decrease the variance and thus improve generalization. As shown in Fig. 1, to aggregate the outputs from LR, KNN, SVM, RT and CNN, the strategy of weighted arithmetic mean was used where the corresponding weights were computed by linear least squares.

2.2. Evaluation Metrics

With a separate dataset, consisting of acromegaly and normal facial photographs, we used several classical metrics to quantify the quality of acromegaly detection: sensitivity and specificity, positive predictive value (PPV) and negative predictive value (NPV), and f1-score, where sensitivity was defined as true positive/condition positive, specificity was defined as true negative/condition negative, PPV was defined as true positive/prediction positive and NPV was defined as true negative/prediction negative. The F1 score can be interpreted as a weighted average of the precision and recall, where the formula for the F1 score is: $F1 = 2 * (\text{precision} * \text{recall}) / (\text{precision} + \text{recall})$.

2.3. Facial Landmarks

General framework of our method to automatically detect acromegaly from facial photographs using machine learning methods are shown in Fig. 3: the most left part showed the training processing, which included face detection and normalization from original input images, facial feature extraction and landmark localization, and face frontalization to improve the accuracy of acromegaly diagnosis; the middle left part showed the model training processing, which included Generalized Linear Models(LM), K-nearest neighbors (KNN), Support Vector Machines (SVM), Forests of randomized trees (RT), Convolutional Neural Network (CNN), and Ensemble Method (EM); the middle right part showed the

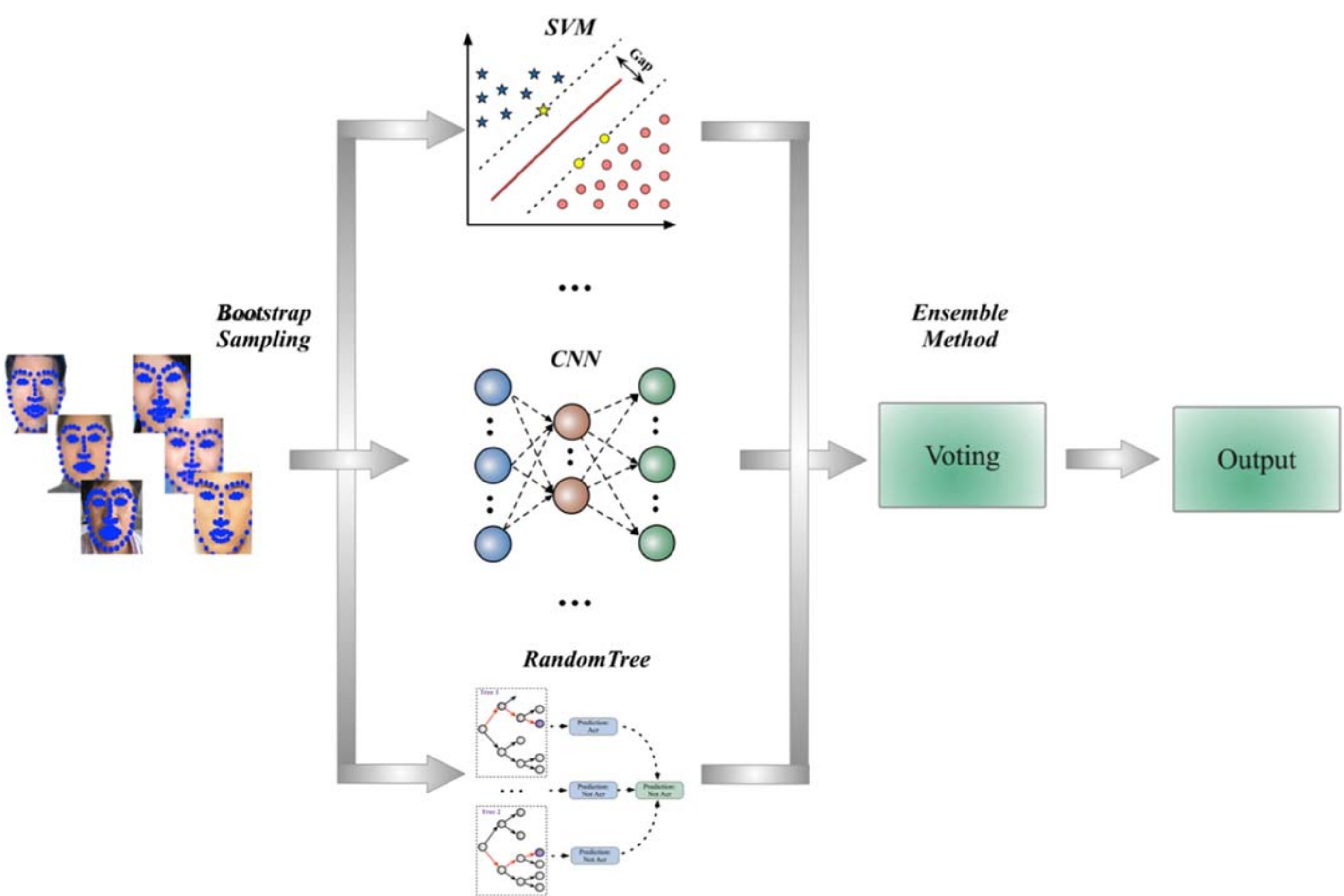

Fig. 1. Ensemble method used to combine the predictions of the basic estimators (LM, KNN, SVM, RT, CNN) to achieve higher classification accuracy as well as better generalizability and robustness for acromegaly diagnosis.

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