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ARTICLE

Evaluation of a computer-based facial dysmorphology analysis algorithm (Face2Gene) using standardized textbook photos

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Abstract

Background Genetic syndromes often have ocular involvement. Ophthalmologists may have difficulty identifying dysmorphic features in genetic syndrome evaluations. We investigated the sensitivity and specificity of Face2Gene (F2G), a digital image analysis software trained on integrating dysmorphic features, by analysing patient photos from genetics textbooks.

Methods We analysed all clear facial photos contained within the textbooks *Smith's Recognizable Patterns of Human Malformation* and *Genetic Diseases of the Eye* using F2G under standard lighting conditions. Variables captured include colour versus grey scale photo, the gender of the patient (if known), age of the patient (if known), disease categories, diagnosis as listed in the textbook, and whether the disease has ophthalmic involvement (as described in the textbook entries). Any photos rejected by F2G were excluded. We analysed the data for accuracy, sensitivity, and specificity based on disease categories as outlined in *Smith's Recognizable Patterns of Malformation*.

Results We analysed 353 photos found within two textbooks. The exact book diagnosis was identified by F2G in 150 (42.5%) entries, and was included in the top three differential diagnoses in 191 (54.1%) entries. F2G is highly sensitive for craniosynostosis syndromes (point estimate [PE] 80.0%, 95% confidence interval [CI] 56.3–94.3%, $P = 0.0118$) and syndromes with facial defects as a major feature (PE 77.8%, 95% CI 52.4–93.6%, $P = 0.0309$). F2G was highly specific (PE > 83percentage with $P < 0.001$) for all disease categories.

Conclusions F2G is a useful tool for paediatric ophthalmologists to help build a differential diagnosis when evaluating children with dysmorphic facial features.

Introduction

There is a myriad of systemic genetic diseases in childhood with eye involvement. Facial dysmorphism is often a key component of syndromes involving the eye [1]. In a tertiary paediatric anterior segment service, 26.5–38% of patients may present with dysmorphic facial features [2]. Making a syndromic diagnosis is a key step in identifying genetic disease that could inform future treatment. However, ophthalmologists usually lack the necessary training in identifying and evaluating dysmorphic features.

Computer-learning algorithms can be used to analyse digital images and aid in the diagnostic process. These algorithms have already proven useful in clinical ophthalmology. Recently, a digital image processing software showed a 92.5% accuracy in diagnosing diabetic retinopathy based on fundus photos [3]. Face2Gene (F2G, FDNA Inc. Boston, MA, USA) is a smart-phone based computerized facial dysmorphology analysis program that analyses 2-dimensional facial images to provide a list of thirty differential diagnoses of syndromes (Face2Gene. https://www.face2gene.com/. Accessed September 10, 2019). Such algorithms are powerful tools in generating genetic syndrome differential diagnoses and may play an increasingly important role in an era of pandemic-driven telehealth delivery. In this study, we assessed the sensitivity and specificity of F2G when used to analyse images of a wide

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variety of genetic syndromes from two popular genetics textbooks.

Subjects and methods

The Face2Gene algorithm was downloaded from the Apple App Store and installed on to an iPhone 9 (Apple Inc., Cupertino, California, United States of America). The algorithm was activated and registered according the manufacturer instructions. Under standard lighting, all clear facial photographs without any hardware (e.g. tracheostomy tube) contained within the textbooks *Smith's Recognizable Patterns of Human Malformation, 7th Edition* and *Genetic Diseases of the Eye, 2nd Edition* were captured and analysed using F2G [3, 4]. Once analysed, the F2G output includes 30 "Suggested Syndromes" listed in the most- to least-likely diagnosis, along with a "gestalt score" for each syndrome. If an age-series of photographs was presented, we used the oldest photograph available for each patient. Variables captured include colour versus grey-scale photo, the gender of the patient (if known), age of the patient (if known), disease categories, diagnosis as listed in the textbook, and whether the disease has ophthalmic involvement (as described in the textbook entries). One photo per patient was included. Any photos rejected by the F2G algorithm were excluded. We analysed the data for accuracy, sensitivity, and specificity based on disease categories as outlined in Smith's Recognizable Patterns of Malformation, 7th Edition due to limited sample size for any single diagnosis.

Results

A total of 353 facial images from the two textbooks were analysed. The top F2G diagnosis matched the book diagnosis in 150 (42.5%) entries, while it is included in the top three in 191 (54.1%) images. Of the 259 entries with ophthalmic involvement, the top F2G diagnosis matched the book diagnosis in 108 (49.4%) entries, while the book diagnosis is included in the top three differential diagnoses in 140 (54.1%) entries. F2G was able to successfully assign images to 21 of the 22 book categories. No single diagnosis occurred in the books more than eight times.

F2G is highly sensitive for craniosynostosis syndromes (point estimate [PE] 80.0%, 95% confidence interval [CI] 56.3–94.3%, $P = 0.0118$) and syndromes with facial defects as a major feature (PE 77.8%, 95% CI 52.4 – 93.6%, $P = 0.0309$). F2G was highly specific (PE > 90% with $P < 0.001$) and demonstrated a significant negative predictive probability (PE > 83 % with $P < 0.0001$) in all 21 categories of disease that it identified. Photograph colour, gender and age did not have any significant correlation to outcomes.

Discussion

The importance of computer-learning algorithm in clinical medicine has been increasing steadily over the past decade, with the first artificial intelligence software for the detection of diabetic retinopathy approved by the U.S. Food and Drug Administration in 2018 [5, 6]. The 2019 coronavirus disease pandemic has hastened the worldwide uptake of telehealth across all clinical specialties [7], and computer-based algorithms such as F2G will likely become increasingly central in the remote diagnosis and management of diseases [8]. This is the first study on using smart-phone artificial intelligence algorithm in the diagnosis of syndromes involving ocular anomalies. We found F2G to be highly specific for assigning patients with dysmorphic features into the 21 categories in *Smith's Recognizable Patterns of Human Malformation, 7th Edition*, suggesting that it may be useful to rule out certain syndrome types in the settings of ambiguous clinical findings and/or history. F2G is highly sensitive for craniosynostosis syndromes and syndromes with facial defects as a major feature, and there was a higher accuracy in the subgroup with eye involvement. This makes F2G particularly suitable for eye care professional to generate syndromic differential diagnoses when an ophthalmic finding is suspected to be a part of a syndromic constellation. Overall, the algorithm had modest accuracy in identifying the book diagnoses both as the top diagnosis and within the top three potential diagnoses, although previous studies have reported high accuracy in using F2G to differentiate between limited numbers of diagnoses based on photos [9–11]. This discrepancy may be due to the breadth of diagnostic spectra tested in this study, and the variable quality/resolution of the standard photographs contained within the textbooks. F2G is designed as a cloud-based application and it is conceivable that with further machine learning using a real-time, evolving database, the accuracy of the program will improve over time.

This study has several limitations. Although lighting conditions were standardized for each image capture, exact positioning, size, and shape of photos varied. Our analysis did not include race, a variable that previous studies have reported to affect F2G's analytical parameters [12]. Last, as smart phone camera resolutions and functions improve over time, our method of "taking the photo of a photo" may not be generalizable to subsequent generations of smart devices. Future studies may focus on the impact of supplemental demographic information on diagnostic accuracy, sensitivity, and specificity. In summary, F2G may be a useful tool for ophthalmologists to generate a reasonable list of differential diagnoses when evaluating a child with suspected syndromes.

Summary

What is known before

- Genetic syndromes are frequently encountered in the paediatric ophthalmology clinic.
- Facial dysmorphoogy recognition is a difficult skill for non-geneticists to acquire.
- Smart-phone based facial recognition algorithm Face2-Gene may be a substitute, but its sensitivity and specific has not been tested with standardized photographs.

What this study adds

- Face2Gene algorithm was highly sensitive for cranio-synostosis syndromes and syndromes with facial feature as a major feature.
- Face2Gene algorithm was highly specific for all disease categories.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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