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The Never-Changing Face Of Fragile X?

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Dr William W. Ireland (1832-1909) was medical superintendent of the Scottish National Institution for the Education of Imbecile Children at Larbert, Scotland in the 1870s and published extensively on matters psychiatric, neurological and historical.^{1,2} In his book, *On Idiocy and Imbecility*, of 1877,³ which came to be considered the definitive work on the topic, he attempted to categorise the aetiologies of individuals who would now be recognised as having an intellectual disability. In his chapter on 'Genetous Idiocy', he notes that, "The most common accompaniment of genetous idiocy, is what has been variously called the keel-shaped, or saddle-shaped, or vaulted palate."

Accompanying this description is a sketch (Figure 1) of an individual with such a vaulted palate, whose face we believe bears a striking resemblance to many individuals with fragile X syndrome. Such 'prima facie' evidence is supported by the fact that arched palates are a common feature in fragile X syndrome⁴, which itself is the most common cause of inherited (or 'genetous') intellectual disability.

Using this sketch of the individual, and the scant clinical information available, the authors used the Face2Gene Clinic Application⁵ to examine the original sketch in the book. On facial features alone, the application returned Mucopolysaccharidosis Type IV, Fragile X Syndrome and Smith-Lemli-Opitz Syndrome as the top three suggested syndromes. Including the known clinical information of 'high palate' and the authors' further observations from the image of 'large forehead' and apparent 'poor eye contact', the application returned Fragile X Syndrome as the most likely diagnosis.

Whilst not conclusive, the authors suggest that this figure appearing in print over 140 years ago may represent one of the earliest depictions of an individual with what has come to be known as fragile X syndrome. The case also highlights the potential value of facial phenotype-to-genotype software in support of clinical diagnostics and demonstrates the possible application of such software to art works more broadly.



Figure 1: Image originally published by W.W. Ireland in 1877

Contributors: AM made the observation noted and prepared the first draft of the manuscript. All authors interpreted the results, provided critical review and revision of the letter, and approved the decision to submit for publication.

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