Quantitative Phenotyping in Intellectual Disability Patients

Intellectual disability (ID) is a common disorder affecting 1% of the general population, yet its cause is heterogeneous. The identification of novel genes responsible for intellectual disability is an ongoing task. We have recently shown that the majority of ID cases are caused by rare sporadic de novo genetic mutations and it is estimated that up to 2000 genes may be linked to intellectual disability. A key strategy for identifying novel intellectual disability genes, is the identification of multiple patients with mutations affecting the same gene.

The development of the human brain is intrinsically linked to the face. Individuals with intellectual disability often have dysmorphic facial features. In healthy individuals inheritance plays a key role in determining the facial features of a child. However in the case of intellectual disability, the impact of a genetic mutation results in patients appearing more similar to other individuals with the same genetic mutation, than their own family e.g. Down syndrome.

To date the technological developments in sequencing have outpaced those in phenotyping. Despite the distinctive, although sometimes subtle facial features, phenotyping of patients is currently a manual and qualitative task. More recently the development of the Human Phenotype Ontology has resulted in the description of patients being stored in a structured language; however phenotyping of patients remains a subjective process. A quick, non-invasive method to capture the features of patient’s faces is needed. To date we have collected 2D photos and structured phenotype information for approximately 5,000 individuals.

The aim of this project is to develop quantitative methods for phenotyping patients, to identify new genes responsible for ID by i) using existing 2D images, and additionally collecting 3D and video images of patients, ii) developing image analysis methods to objectively extract features and hence phenotype patients, before iii) developing heuristics to measure and identify patients with similar facial features for which followup genetic testing can be performed.

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