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## **Brain Pathologies and Big Data**

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We now know that a single gene mutation may present with multiple phenotypes, and vice versa, that a range of genetic abnormalities may cause a single phenotype. These observations lead to the conclusion that a deeper understanding is needed of the way changes at one spatial or temporal level of organisation (e.g., genetic, proteomic or metabolic) integrate and translate into others, eventually resulting in behaviour and cognition. The traditional approach to determining disease nosology- eliciting symptoms and signs, creating clusters of like individuals and defining diseases primarily on those criteria has not generated fundamental breakthroughs in understanding sequences of pathophysiology mechanisms that lead to the repertoire of psychiatric and neurological diseases.

It is time to radically overhaul our epistemological approach to such problems. We now know a great deal about brain structure and function. From genes, through functional protein expression, to cerebral networks and functionally specialised areas defined via physiological cell recording, microanatomy and imaging we have accumulated a mass of knowledge about the brain that so far defies easy interpretation. Advances in information technologies, from supercomputers to distributed and interactive databases, now provide a way to federate very large and diverse datasets and to integrate them via predictive data-led analyses.

Human functional and structural brain imaging with MRI continues to revolutionise tissue characterisation from development, through ageing and as a function of disease. Multi-modal and multi-sequence imaging approaches that measure different aspects of tissue integrity are leading to a rich mesoscopic-level characterisation of brain tissue properties. Novel image classification techniques that capitalise on advanced machine learning techniques and powerful computers are opening the road to individual brain analysis. Data-mining methods, often developed in other data-rich domains of science, especially particle and nuclear physics, are making it possible to identify causes of disease or its expression from patterns derived by exhaustive analysis of combinations of genetic, molecular, clinical, behavioural and other biological data. Imaging is generating data that links molecular and cellular levels of organisation to the systems that subtend, action, sensation, cognition and emotion. These ideas will be illustrated with reference to the human dementias.

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