The Lothian Birth Cohort 1936 and Edinburgh's clinical research infrastructure: searching for genetic and imaging biomarkers

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Introduction

Identifying the determinants of cognitive aging is a research priority. It is ideal to have a measure of mental efficiency from youth, but few studies have this. Scotland is special; it collected mental test data on almost everyone born in 1936 at age 11 in the Scottish Mental Survey of 1947. The Lothian Birth Cohort 1936 Study has traced and re-tested 1091 of these individuals to find out why some people do worse or better than expected from their ability at age 11 in 1947.

Background

Genetic and imaging biomarkers in combination with cognitive changes over 60 years and lifestyle factors, are key to understanding the processes at work in the ageing brain and how they can be mitigated to ensure successful cognitive ageing. Multidisciplinary research such as this is facilitated in **Edinburgh** by the existence of centres like **WTCRF** and **SBIRC**. These centres allow investigators access to the specialized equipment and experienced staff necessary for the effective running of studies.

Figure 1: Measuring blood vessel bifurcation geometry in a retinal fundus image. Arterial values in white and venular values in black.

Methods

Study participants at age 70 and 73 years attended the **Edinburgh WTCRF**, a unique environment for the support of clinical research. With the **research nurses** they completed a battery of cognitive and physical tests, gave details of their medical history and social background and completed detailed psychosocial questionnaires. Blood samples were collected for DNA and biomarker analysis by the **Genetics Core** laboratory. Retinal photographs of both eyes were taken with a digital retinal camera for analysis supported by the **Image Analysis Core**. The participants also underwent detailed MR brain imaging at **SBIRC**.

Figure 2: Senior Radiographer Iona Hamilton pictured with the SFC Brain Imaging Research Centre (SBIRC) research 1.5 T GE Signa MRI scanner.
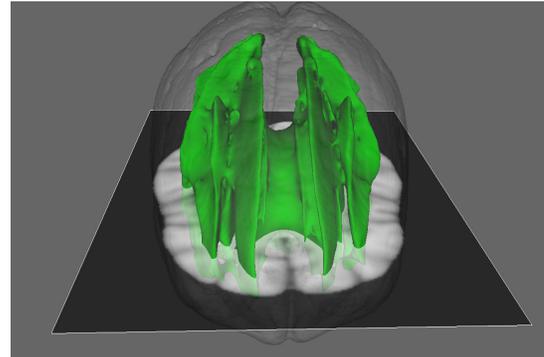

Figure 3: volume rendering of an MR scan for a study participant. The green area is the white matter; this is the "brain wiring" i.e. the connections between the various parts of the brain.

Results

Most analyses are ongoing. What follows are a few examples.

Genetic analysis: A genome wide association study using the Illumina Human610-Quad chip was performed at the **Genetics Core**. Common variants in 3 genes were found to be related to activated partial thromboplastin time (aPTT), a marker for risk of thrombosis and coagulation disorders.

Image analysis: Retinal microvasculature abnormalities were quantified by computational post-processing methods developed in the **Image Analysis Core** to be tested as biomarkers for the state of the cerebral microvasculature. Investigation is on-going to explore possible relationship to cognitive ability level or change.

Imaging: Structural MR, diffusion tensor, magnetization transfer and T1-mapping techniques are being used to measure many factors, with special focus on the integrity of the brain's white matter in old age.
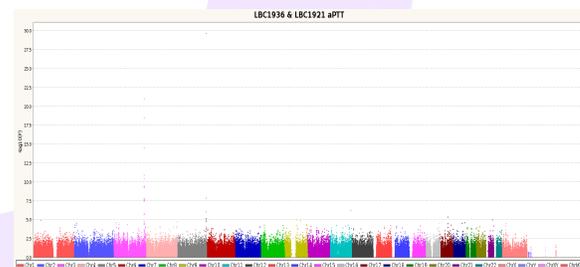

Figure 4: Manhattan plot showing significant associations of relatively large effect size between aPTT and SNPS in three genes. Taken from *Am J Hum Genet*. 2010; 86(4):626-31

Conclusions

To understand the processes at work in the ageing brain (with the long-term aim of providing information to help interventions to promote successful cognitive ageing) an integrated and multidisciplinary approach is essential, including genetic and imaging biomarkers, detailed lifestyle and psychosocial information and cognitive ability assessments across the lifecourse.

Such research is facilitated by the existence of centres like the **Edinburgh WTCRF** and **SBIRC**.

Acknowledgements