

Date of submission: 31 October 2012 1

Project title: 1

Applicant: Dominic Job

Centre for In Vivo Imaging Sciences PhD Project Proposal Template for PhDs starting in 2013

Centre (i.e. primary facility/centre/unit to which this studentship will be attached*):

Brain Research Imaging Centre, Neuroimaging Sciences, The University of Edinburgh

First supervisor: contact details

Name: Dr Dominic Job

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Second supervisor: contact details

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Dr David Rodriguez Gonzalez

Informatics Forum

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Speciality/discipline of first supervisor:

Neuroinformatics and Computer science

Speciality/discipline of second supervisor:

Geriatric medicine/
Informatics (Data intensive research)

PROJECT

Title:

A quantitative diagnostic method incorporating brain images and clinical measures

Likely background of suitable student (eg. Biomedical Science, Cardiovascular Biology, Engineering, Informatics, Image Analysis, Mathematics, Lay, Art, Neuroscience, Medical Physics, Chemistry, Psychology) and essential skills required prior to starting this PhD:

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The project would suit a student with strong statistical skills and a background in Neuroinformatics, Neuroscience, or Psychology but also potentially a student from a pure Statistical, Mathematical, or Engineering background and an interest in brain ageing and pathology. It requires understanding of statistical analyses and summaries (e.g. hypotheses testing, means, and percentiles), clinical and brain image data, the sensitivities and management of these data; and the ability to work as part of an interdisciplinary group of researchers. There will be additional mentorship from Prof Joanna Wardlaw (expertise in neuroimaging).

*usually this would be the university in which the first supervisor is based.

Summary of proposed project (approximately 200 words):

Brain structure and clinical measures, e.g. blood pressure, change with age. Although associations have been found between brain structure and clinical measures, there is no standard, quantitative method for determining “how normal” individual patient brain scans and associated clinical measures are, e.g. what are the normal levels and limits of grey matter volume given different blood pressures at different ages? Templates of normal brain structure exist but they require qualitative assessment by clinicians. Further, these templates have been developed with relatively few subjects mostly at younger ages and have not incorporated clinical data. Given that: i) normal ageing is associated with a wide range of brain structure; ii) values of clinical measures may affect the “normality” of brain structure; and iii) the experience of different clinicians (radiologists, neuroradiologists, general physicians) may lead to different interpretations of images; a quantitative method for diagnosing brain scans and clinical measures together is required. This would then need to be evaluated to assess whether it is clinically useful. This method may also be used by other researchers to ensure their controls are appropriate, i.e. not skewed to one side of the normative range.

This work will build on the Brain Images of Normal Subjects (BraINS) bank that is compiling the required data, and collaborate with all members of this team, and potentially with other brain banks internationally. The aims of the proposed work are to: 1) combine and summarise large volumes of normal brain image and clinical data; 2) develop a system to read new patient data and produce a single “rank of normality”; 3) test whether this system is clinically useful; and 4) determine the significance of normality ranks, e.g. whether or not they predict disease.

Key references (up to five):

1. Dickie, D.A., et al. (2012). Do brain image databanks support understanding of normal ageing brain structure? A systematic review. *Eur Radiol.* 22, 1385-1394.
2. Farrell, C., et al. (2009). Development and initial testing of normal reference MR images for the brain at ages 65–70 and 75–80 years. *Eur Radiol.* 19, 177–183.
3. Mazziotta, J.C., et al. (2009). The myth of the normal, average human brain - the ICBM experience: (1) Subject screening and eligibility. *Neuroimage.* 44, 914-922.
4. Freedman, D. (2010). *Statistical Models and Causal Inference: A Dialogue with the Social Sciences.* Cambridge University Press, Cambridge.
5. Breteler, M., et al. (1994). Cerebral white matter lesions, vascular risk factors, and cognitive function in a population-based study. *Neurology.* 44,1246-1252.

In what way does this PhD proposal meet the CIVIS criteria as described in the call for proposals? (50 words)

This proposal will develop an imaging tool to address an important research question, the accurate interpretation of brain scans and clinical measures in older people, both for clinical use and to allow researchers to select appropriate control subjects. It involves multidisciplinary collaboration among neuroimaging, medicine, computer science and informatics (data intensive research) centres.

**Please state which scheme your proposal should be considered for:
If you are unsure please discuss with named individual.**

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- UoE CMVM (Prof J Wardlaw, Prof I Marshall, Prof M Holmes, Prof E van Beek)
- UoE CHSS PPLS Psychology (Prof R Logie)
- UoE CSE Informatics DTC (Prof D Robertson)
- HWU Engineering (Prof Rory Duncan)