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Improving data availability for brain image biobanking in healthy subjects: Practice-based suggestions from an international multidisciplinary working group

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ABSTRACT

Brain imaging is now ubiquitous in clinical practice and research. The case for bringing together large amounts of image data from well-characterised healthy subjects and those with a range of common brain diseases across the life course is now compelling. This report follows a meeting of international experts from multiple disciplines, all interested in brain image biobanking. The meeting included neuroimaging experts (clinical and non-clinical), computer scientists, epidemiologists, clinicians, ethicists, and lawyers involved in creating brain image banks. The meeting followed a structured format to discuss current and emerging brain image banks; applications such as atlases; conceptual and statistical problems (e.g. defining 'normality'); legal, ethical and technological issues (e.g. consents, potential for data linkage, data security, harmonisation, data storage and enabling of research data sharing). We summarise the lessons learned from the experiences of a wide range of individual image banks, and provide practical recommendations to enhance creation, use and reuse of neuroimaging data. Our aim is to maximise the benefit of the image data, provided voluntarily by research participants and funded by many organisations, for human health. Our ultimate vision is of a federated network of brain image biobanks accessible for large studies of brain structure and function.

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Introduction

Neuroimaging has become embedded in substantial research endeavours to understand normal brain function and effects of disease (e.g. Thompson et al., 2003; Fox and Schott, 2004; Lemaitre et al., 2005; Marcus et al., 2009; Wardlaw et al., 2011a, 2011b; Weiner et al., 2015). Until recently, many neuroimaging studies were in single centres and, inevitably, of modest size (Dickie et al., 2012). Many much larger population scanning initiatives are now ongoing (Jack Jr et al., 2008), and many multicentre clinical trials routinely include imaging as part of inclusion criteria and as outcome measures (Cash et al., 2014), providing the potential for large multicentre collections capturing the range of brain structure in the population. The importance of maximising the value captured in this large amount of imaging data – to detect how differences in brain structure and function relate to behavioural or clinical outcomes – is now widely recognised (Toga, 2002; Barkhof, 2012; Poline et al., 2012). The value of data for answering new questions can grow with sample size, e.g. for replication, increasing population representativeness, and increasing study power. To address this issue, a growing number of electronic databanks including brain imaging are available, either from dedicated cohorts (e.g. Alzheimer's Disease Neuroimaging Initiative, UK Biobank, IMAGEN), or collections of studies (e.g. Brain Imaging in Normal Subjects, Dementia Platform UK, Open Access Series of Imaging Studies): see Table 1.

Brain images from 'healthy' subjects are important

The wide variation in brain structure and function both within and between individuals at different ages has long been recognised (Wardlaw et al., 2011a, 2011b; Dickie et al., 2013). Methodologies that use appropriately representative populations are needed to provide normative populations, particularly for healthy subjects (i.e. those without neurological diseases such as stroke or dementia). They can provide informative reports for users (e.g. 'brain on 5th percentile for volume at age 70' for a specified population) and simultaneously embrace the spectrum of individual variation (Dickie et al., 2015a, 2015b). Brain imaging is increasingly used in the diagnosis of neurological diseases, and mental health disorders (Fox and Schott, 2004). Data from existing cohort or population studies (e.g. Marcus et al., 2009), can help define boundaries between health and disease, to aid diagnosis and trial inclusion, to provide effect size estimates for planning trials, and, where relevant, controls for case-control studies (e.g. Dickie et al., 2015a; ADNI: Potvin et al., 2016).

Current status of brain imaging banks

Large repositories of brain imaging data from well-characterised subjects in accessible databanks are required to achieve this, while ensuring that data protection concerns are also addressed. These comprise data initiatives that are planned around harmonised protocols, such as ADNI (Alzheimer's Disease Neuroimaging Initiative) (Weiner et al., 2015), UK Biobank (Matthews & Sudlow, 2016), Human Connectome Project (van Essen et al., 2013), OASIS (Open Access Series of Imaging Studies) (Marcus et al., 2007a, 2007b, 2009), and those that represent data aggregation without initial harmonisation e.g. ENIGMA. (Enhancing Neuro Imaging Genetics through Meta-Analysis - Thompson et al., 2014, 2015). The value of brain images is hugely enhanced by the information on the characteristics of individual subjects and the study in which they participated, but at present studies vary widely in what data they present on the study, subject or image data, and how these data are presented (Dickie et al., 2012).

Only a small proportion of the images performed for research are included in biobanks, and in existing structural brain image biobanks, normal subjects over 60 years of age are relatively under-represented, with limited cognitive and medical metadata to support their classification as "normal" (Dickie et al., 2012), and available with a limited range of neuroimaging sequences. For example, fluid attenuated inversion recovery (FLAIR) and T2* volumes are often not available, although they are essential for sensitively identifying and quantifying white matter hyper-intensities (WMH) and microbleeds respectively, neuropathologies present in normal ageing but associated with vascular cognitive impairment (Wardlaw et al., 2013; Ritchie et al., 2016). Newer initiatives like BRAINS (Job et al., 2016) provide a range of

Table 1
Databases presented at brain image bank meeting with relevant references, website, and data access policy.

Data base	Website	Data access policy
ADNI (Weiner, 2015)	http://adni.loni.usc.edu/	ADNI: registration and application for approval by steering committee for data access
ENIGMA (Thompson et al., 2015)	http://enigma.ini.usc.edu/	ENIGMA: data is shared between members on an ad hoc basis
BRAINS (Job et al., 2016)	http://www.brainsimagebank.ac.uk/	Open access search of available data; registration and application for approval by steering committee for data access
Dementia Platform UK (DPUK)	http://www.dementiasplatform.uk/	In development: online registration required
Edinburgh Birth Cohort	www.ebc.ed.ac.uk	Online search of available data; registration and application for approval by steering committee for data access via http://www.brainsimagebank.ac.uk/
European Population Imaging Infrastructure	http://populationimaging.eu/	Email contact for information on available datasets
Rotterdam study (Ikram et al., 2015; Hofman et al., 2015)	http://www.erasmus-epidemiology.nl/research/ergo.htm	
Generation R (Jaddoe et al., 2012)	http://www.generationr.nl/	
EVA, 3-CITIES, DBGIN, BIL & GIN, i-SHARE (Alperovitch et al., 2002; Lemaitre et al., 2005; Mazoyer et al. 2016).	http://www.gin.cnrs.fr/BILandGIN http://www.three-city-study.com/the-three-city-study.php	Registration and application for approval by steering committee for data access
IMAGEN	http://www.imagen-europe.com/en/consortium.php	Registration and application for approval by steering committee for data access
Montreal Consortium for Brain Imaging Research (Evans et al., 2012).	https://www.mcgill.ca/globalhealth/international-consortium-brain-mapping	Registration and application for approval by steering committee for data access
OASIS (Marcus et al., 2007b, 2009)	http://www.oasis-brains.org/	OASIS: open access, no registration required
Human Connectome Project (Van Essen et al., 2013)	http://www.humanconnectome.org/	HCP: open access with restricted access for sensitive data (registration and application for approval by steering committee)
Rhineland study	https://www.dzne.de/en/research/research-areas/population-health-sciences/rhineland-study.html	Email contact for information on available datasets
UK Biobank (Matthews and Sudlow, 2015)	http://www.ukbiobank.ac.uk/	Open access search of available data; registration and application for approval by steering committee for data access