Work Package 13: Brain Donation

UK Brain Bank Capacity & a Strategy for DPUK Brain Donation

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Executive Summary

1. This report relates to DPUK Work Package 13 Objective 7: To establish a brain banking strategy based on capacity and scientific value.

2. The report presents quantitative and descriptive data relating to the current capacity and workload of 10 UK brain banks, evaluates options for extending brain donation to DPUK cohorts and makes recommendations for a longer term brain donation strategy.

3. Currently there is little spare capacity available across the UK Brain Bank Network.

4. Across the brain banks there are significant differences in the proportion of ad hoc vs registered brains collected.

5. Estimates of the number and characteristics of participants to be consented to brain donation through DPUK are required in order to predict the impact of DPUK with greater precision.

6. The availability of mortuary services is a potential bottleneck & there is a need to engage with NHS Trusts.

7. Clarification of scientific questions and identification of what DPUK seek to learn from donated brains would help to shape a brain donation strategy.

8. Conditional support for a UK Biobank brain donation pilot study.

9. A decentralised model based upon the accommodation of extra DPUK activity within existing brain bank infrastructure across the 10 brain banks is favoured.

10. The long term suitability of alternative models for consenting, centralised collection and storage warrant exploration.

Introduction

This report relates to Objective 7 of DPUK Work Package 13: Brain Donation. Objective 7 is to establish a brain banking strategy based on capacity and scientific value. In order to develop a brain banking strategy, a capacity questionnaire was developed in collaboration with the MRC UK Brain Bank Network (See Appendix 1). The questionnaire was completed by the 10 Brain Banks in the Network during June 2015. The aims of the questionnaire were i) To measure the current capacity of Brain Banks and ii) To evaluate options for enhancing the capacity of brain banks in relation to the DPUK Cohort. Capacity data relates the period 1st January 2014 – 31st December 2014.

Brain Bank	Information provided by
South West Dementia Brain Bank	Prof Seth Love, Dr. Laura Palmer, Prof Patrick Kehoe
Edinburgh Brain and Tissue Banks	Dr. Colin Smith
Newcastle Brain Tissue Resource	Debbie Lett
Thomas Willis Oxford Brain Collection	Marie Hamard, Dr. Olaf Ansorge
London Neurodegenerative Diseases Brain Bank	Dr. Claire Troakes
Cambridge Brain Bank	Beverley Haynes
Manchester Brain Bank	Prof David Mann, Andrew Robinson, Steve Chew-Graham
Queen Square Brain Bank	Linda Parsons, Lynn Haddon
Sheffield Brain Tissue Bank	Gill Forster
Multiple Sclerosis and Parkinson's Tissue Bank	Dr. Djordje Gveric

The report is divided into 3 sections. The first section summarises quantitative and descriptive data relating to the current capacity and workload of the brain banks. In the second section, the capacity of the BBN is considered in relation to DPUK brain donation and options for enhancing capacity are evaluated. The third section outlines a strategy proposed by the DPUK Executive for a pilot brain donation study, provides a summary of responses in relation to this proposal and presents recommendations for a longer term brain donation strategy.

Section 1: Current Capacity & Workload

Table 1: Brain collection & donation source

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
No. Control brains	9 (+ 2 pending)	21	11	7	15	4	19	3	**	18
No. Diseased brains	30	61	41	69	107	51	31	55	14	95
Total Brains Processed	**41**	**82**	**52**	**76**	**122**	**55**	**50**	**58**	**14**	**113**
Cohort brains	15 (38%)	61 *(100%)	30 (58%)	45 (59%)	38 (31%)	6 (11%)	34 (68%)	2 (3%)	3 (21%)	2 (2%)
Register brains	12 (31%)	61*(100%)	11 (21%)	2 (2.6%)	44 (36%)	27 (51%)	14 (28%)	48 (83%)	0 (0%)	105 (91%)
Ad hoc brains	12 (31%)	0 (0%)	11 (21%)	29 (38%)	40 (33%)	20 (38%)	2 (4%)	8 (14%)	11 (79%)	8 (7%)

* Cohort studies also on clinical register, ** Blind regarding CFAS Diagnosis so may include controls

Table 2: Brain collection & diagnoses

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
PSP	1		3	1	5	8	2	13		
AD	13	5	12	21	46	16	19	6	1	
AD Mixed			8	6	2					
Globular glial taupathy	1							2		
PD/PDD	2		3	2		2		8		
PD/LBD				11					1	
Parkinsons										70
FTLD/FTD	1			1	15	3	2	5	1	
Argyrophilic grain disease	1			3	2					
Vascular Dementia	1			2						
Cerebrovascular disease	1		2	2	4	2	1			
Intracerebral haemorrhage		26		2						
Cerebral haemorrhage				19		1				
MND		8	2	1	10	5	2	3	5	
CJD		22							1	
Mitochondrial disease			3							
Rare neurological			4							
DLB			1		7	3	5	1		
Huntingtons Disease			1		3					
MCI			1							
Psychiatric (schizo.)			1							
Head Trauma					1				1	

Other (MSA, CBND, MS etc)				3	12					
Down Syndrome						2				
Striato degeneration						1				
ME						2				
RH cohort no diagnosis (given to CBB)						6				
Chronic Traumatic Encephalopathy								1		
Corticobasal degeneration							2	5		
Leukodystrophy								1		
Multiple system atrophy				1			2	11		
MacLoud Syndrome									1	
CFAS									3	
MS										25
Autism				2						
Tumour				5						
Awaiting histological diagnosis	9									
TOTAL	**30**	**61**	**41**	**69**	**107**	**51**	**35**	**43**	**14**	**95**

Table 3: Total donations & source

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
Cohort										
BDR	15		16		32		20			
MND		✓								
ALZ		✓								
ICH		✓								
CJD		✓								
COGFAST			1							
CFAS			1			6			3	
Harlow series			1							
Health Ageing			1							
ICICLE-PD			3							
Jules Thorn Imaging study			6							
MRI and Brain mapping in depression			1							
OAP/Biomarkers/IOP					2					
KCH MND clinic					2					
Dementia Research Group, UCL					2					
Manchester and Newcastle Longitudinal Ageing Cohort							14			
Cambridge Repair Cohort								1		
Prof Huw Morris Cohort								1		
Total Cohort	15	61*	30		38	6	34	2	3	2
Register										
NBTR-Mitochondrial			3							
NBTR-MND			2							
MCI - Control Initiative			2							

NBTR-other			4							
CFU							14			
Total Register	**12**	**61***	**11**		**44**	**27**	**14**	**48**		**105**
Ad Hoc										
Ad Hoc (General)	12	0	7		40	20	2			
Ad Hoc (Control Initiative)			4							
Ad Hoc Total	**12**	**0**	**11**		**40**	**20**	**2**	**8**	**11**	**8**
TOTAL	**41***	82	52		122	53	30	58	14	115

* Cohort participants also on clinical registers,

Table 4: Ongoing commitments to cohorts

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS & PD
BDR	n=406		✓	✓	✓		✓			
Scottish Alzheimer Disease Cohort		✓								
Scottish MND Cohort		✓								
Scottish MS Cohort		✓								
Lothian 1936 Birth Cohort		✓								
National CJD Surveillance Unit		✓								
Lothian intracerebral		✓								
Local Clinical Cohorts			✓							
CFAS I & II			✓			✓			✓	
BioMOx				✓						
OAP/Biomarkers/IOP					✓					
KCH MND clinic					✓					
Dementia Researcg Group, UCL					✓					
Later Life Study						✓				
JH Dementia Study						✓				
Manchester & Newcastle Longitudinal Ageing Cohort							✓			
Cerebral Function Unit Cohort							✓			
Cambridge Repair Cohort								✓		
Prof Huw Morris Cohort								✓		
PINE (Aberdeen)										✓
Discovery (Oxford)										✓
Proband										✓
ICICLE										✓
Register										
NBTR-Mitochondrial			*3*							
NBTR-MND			*2*							
MCI - Control Initiative			*2*							
CFU							14			
SWDBB	n=224									

Table 5: Current staffing levels

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
Director of pathology								0.1		
Director							0.4	0.1	0.5	
Manager	1*	1	1	2 (1 BDR/1 Other)	1	0.2	0.5			1
Lead Technician	1*						0.5			
Technician	1*	2	2.1		2*/**	1	0.2	3		4
Senior Research Nurse		1								1
Nurse			2			1		0.5	* NHS MND nurses	
Biomedical Scientist			1							
Research worker/administrator					1					
Administrator						0.4		1		1
Recruitment Co-ordinator							0.8			
Consultant Neuropathologists							0.2			
Neuropathologist						0.3		0.5	0.5	
Lab manager								1		
Clinical Fellow								0.5		
On call						9K pa				
Tissue co-ordinator				1					0.8	
Data Manager								1		

*Externally funded **BDR funded (Where specified)

Table 6: Brain tissue storage

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
Storage			1500	6,500	2500		890 part brains	2435 (100% fixed and 80% frozen)	1008	1600 (Brain and spinal cord)
Frozen Tissue	642	7 freezers (Since 2005)		1,500	2000 with accompanying frozen	1293 Brains/741 CSF	600 in frozen tissue in 5 freezers		577	
Cerebrospinal fluid	497									
Wet formalin-fixed tissue	849				899	1000			753	
Paraffin embedded blocks	864	Paraffin blocks since 2005		8000	2500 fixed blocks	22,600			920	
Stained tissue sections	870									
Precut unstained tissue	468									
		Frozen samples (10 freezers)								
		Approx 500 Formalin fixed brains, paraffin Blocks (since 1991 onwards)								

Table 7: Criteria for accepting donations

Donation acceptance criteria	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Squar	Sheffield	MS & PD
Cohort criteria (e.g. CFAS, BDR, ALS.AD/PD)	✓		✓	✓	✓		✓		✓	
Donation time limit						>36 hours		>96 hours		?
Coroner involvment/Procural Fiscal Investigation		✓			✓					
Extended Post- Mortem time	BB +72hrs BDR +100hrs		✓	✓	✓					
Post mortem interval		✓							If >72 hrs no frozen tissue	
Interval between time alive & found dead		✓								
Mortuary availability					✓					
Conditions not in research remit	✓							✓		
Disease duration <2 years								✓		
Controls >70yrs (Unless BDR)				✓						
Storage of diseased	✓							Refridgeration within 4 hours		
Brain metastases	✓							✓		
Large haemorrhagic stroke	✓							✓		
Severe hypoxia								✓		
Cause of death	✓									
Other reasons for damaged tissue	✓			✓				✓		
High risk disease	✓							✓		
Transmissible diseases diagnosis	✓									
Level of clinical information		✓		✓	✓				✓	
Rarity of disease					✓					
Family history of disease					✓					
Location of donation						✓				
Common sense & sensitivity							✓			
Consent before death				✓						

Table 8: Number of brains declined

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
Missed donations	8									
Declined donations		2		1	39	0	10	<10	0	
Cohort			0							
Registered	3		0							
Ad hoc	No record		2					Majority		

Table 9: Additional brain processing & storage capacity

Brain Bank	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
Spare capacity (Brains per month)	1 or 2 (If decline ad hoc)	1	2 to 4	None	None	3	None	None	4	20
Spare storage	Yes	No	No	No	No	No	No	No	Limited wet and frozen	No
Room temperature	Approx 400 donations			No					Large capacity paraffin blocks but cardboard	
Freezer	Approx 200-300			2 (Contingency)	1 freezer for next 12 months donations					

Table 10: Estimated workload to manage 10 new donor registrations

	South West	Edinburgh	Newcastle	Oxford	London	Cambridge	Manchester	Queen Square	Sheffield	MS and PD
10 New Donor Registrations	7.5 hours (1 member)		30 hours (Nurse)	40-60 hrs*	5 hrs	20-45 hrs (Home/clinic)		20 hrs	**	35 hours (Administrator)
At donation			40 hrs admin/co-ord	5 hrs Tissue Booking						
			40 hrs Technician	15 hrs Tissue sampling						
			60 hrs Neuropathology	70 hrs Tissue processing etc						
			300 hrs BS							
Overall Total			**470 hrs**	**140 hrs (3 staff)**			**2.5 months**			

***Includes consent taking and donation management including arranging transport and retrieval ** Managed elsewhere**

Capacity Summary

The total number of brains collected in each bank ranges from 14 to 122 and the majority of processed are diseased (n=558, 85%). Donations are largely through cohorts and registers, although ad hoc donations represent a significant source of donations in 4 brain banks (ranging from 33% to 79%) of the total brains collected. Half of the brain banks report no changes in the respective proportions of donations received from cohorts, registers and ad hoc sources in the past 3 years. Some banks report a shift towards registration the availability of increased pool of donors. Reasons specified for this include ageing cohorts, nationwide publicity and referral from 3rd parties (e.g. anatomy departments, Brain Banks, other donor banks). Some banks report a shift away from ad hoc donations and the adoption of acceptance criteria. These included i) the level of clinical data available, ii) research value and iii) available staffing levels and resources. The value of ad hoc donations was emphasised in relation to the opportunity to collect scientifically interesting cases, acting as a last resort for donations declined elsewhere and providing a source of comfort for relatives.

Variation is evident between the Brain Bank Network (BBN) in respect of the use of service support costs. Service support costs are used to pay NHS costs (e.g. body transport, tissue retrieval costs levied by NHS mortuary, processing, cutting, staining and reporting). However, in some cases the costs of returning donated tissue to laboratory for processing, ranging from £50-150 per donation depending on distance, are not covered. In essence, the limit on total service support costs implies that any further increases in the level of brain donation or increases in costs (e.g. mortuary costs rising to £100 per donor) implies a reduction in funding per donation. Furthermore, in order to maintain current capacity, several banks highlighted the need for additional staff including administrators, technicians, mortuary staff, and neuropathologists. As a result of staff shortages, in some banks staff perform multiple roles leading to delays and difficulties.

Job roles vary across the BBN and due to differences in core funding some staff are directly employed by banks and others are employed externally through the MRC or cohorts. For example, in 1 bank the funding of a .5 FTE BMS and 2 sessions of Neuropathologist time are not covered in core funding and reflect increased activity within bank above the level initially funded. In another bank, other than service support costs, there is no specific funding for running the bank and consequently a 0.8 FTE. Tissue Co-ordinator is funded through 1 cohort while working unfunded across several other cohorts. Some banks relay upon NHS staff such as clinic nurses, to identify potential donors, send out information, organise signing consent paperwork, transfer deceased to mortuary and to co-ordinate brain retrieval.

At the point of donation, the brain banks produce clinical summaries to accompany the brain tissue. The level and methods employed for clinical data acquisition vary across the

BBN but in general, the process is dependent upon the donation source as well as the individual circumstances of the donation. Clinical information is therefore routinely collected either within the context of cohort participation or through the registration process (e.g. Information from GP and participant) and annual assessment by the Brain Bank in some cases (e.g telephone assessment of controls). For ad hoc donations, data sources may include clinic records, medical records, retrospective interviews, conversations with referring clinicians/GPs/families, referral letters and police reports.

While there is some uniformity across the BBN in respect of the criteria employed to accept or to decline a donation, each bank may also use cohort specific criteria or modify exclusion criteria in accordance with available resources and individual circumstances. For example, 1 bank was prepared to extend the 72 hour PM delay depending on the level of previous time and effort inputted in assessing the participant and as a commitment to the family. Equivalent modifications were less likely for ad hoc donations unless there was overwhelming evidence of the value of the donation.

Overall, with the exception of London and Manchester, declining donations is relatively rare across the Network. The most common reasons for declining donations include:

- Coroner autopsy referral leading to delay >72 hours
- Prolonged PMI
- Long PM delay
- Clinical exclusion (Brain metastases/tumour/radiotherapy)
- Agonal state
- Registration as full body donor
- Unable to transport donor
- Unable to perform retrieval and return to local area before funeral.
- Lack of clinical information
- If risk posed to staff
- No clinical cognitive data for >70.

The declining process itself largely operates on a case by case basis. In general, i) potential donors are informed that donation not always guaranteed, ii) All donations are considered and not usually declined unless first contact with bank greater than 72 hrs since death, iii) Relatives are assured that bank will do all it can to enable donation to proceed and iv) Family is reassured that they have done everything in their power to carry out their loved one's wishes.

The job title of staff members nominated to decline donations varies between banks and may be the Principal Investigator, Brain Bank manager, Senior Research Nurses, Tissue Coordinator, recruitment co-ordinator, a trained individual from the clinical or bereavement team, an unspecified team member or the referring clinician. The decision process varies in length, but 1 bank aims to inform families of the donation decision within 2 hours. The process entails obtaining relevant information (lasting at least 1 hour) and is team based decision potentially involving consultation with other Brain Banks, GPs, funeral directors and

the local mortuaries. Given the sensitivity of process, estimating the duration of 'declining conversations' is problematic with some families being less accepting than others and requiring significant 'pastoral' care. One bank reported that speaking to the families generally lasted between 10 to 60 minutes (or longer), depending on time required to explain the reasons and to answer questions.

Although the number of declined ad hoc donations is not routinely recorded, 4 of the banks anticipate an increase in the number over the coming years. Reasons specified include: i) Priority (based on staffing and financial considerations) being given to donation from participants who have undertaken regular clinical assessment, ii) An increasing number of ad-hoc donor requests due to increased public awareness of brain donation, iii) An increased number of ad-hoc donor requests from families who have no clinical follow-up, and iv) Restricted mortuary space.

Additional Workload from 10 new donor registrations

Estimates focusing solely on the administrative workload of managing 10 new donor registrations ranged from 5 to 45 hours. Factors influencing the length of registration process included the number and nature of donor enquiries, the location of registration (clinic, telephone or home based) and whether the distribution of forms to third parties, such as GPs, was required. Staff specified to perform this role included administrators, nurses, technicians or a 'team member'. In addition, this role was not always performed by staff exclusively funded by the Brain Bank (e.g. NHS MND nurses). Estimates for 10 new donor registrations which included additional components of the donation process were inevitably longer.

Section 2: Brain Banking Capacity & DPUK

The implications of DPUK for the capacity of brain banks will be determined by a number of factors. These include i) The number and nature of cohort participants to be consented, ii) the number of banks identified to accept DPUK registrations and donations, iii) The registration and consenting method, iv) The acceptance/declining criteria adopted and v) The methods employed for tissue processing, storage and distribution. The BBN was asked to consider options for enhancing the capacity of brain banks in relation to DPUK.

Spare Capacity

A total of 4 banks in the network indicated that they were operating at full capacity and were not currently able to process any additional brains. A further 5 banks reported sufficient capacity to process up to 4 additional brains per month, although in some cases this would imply declining ad hoc donations. However, only 2 of the banks reported the availability of additional storage capacity.

Capacity Constraints

The BBN reported a range of constraints on capacity. These included:

1. Staffing levels including administrators, technical staff, nurses, neuropathology consultant time (to undertake PM and to review histology/reporting time), Tissue collection processing costs
2. Availability of mortuary services
3. A national shortage of consultant neuropathologists and trainees, with most engaged in full time NHS positions with limited interest in supporting this type of activity.
4. Current performance targets
5. Limited tissue processor capacity
6. Large geographical region covered by the bank
7. Unpredictable workload – timely management of new donations and tissue requests
8. Database management support
9. Storage space (e.g. staff, data and tissue sample storage)
10. Additional equipment, laboratory consumables and reagents for histological diagnosis and servicing costs
11. Current large volume of tissue requests vs time to process more donations
12. Undertaker fees

Additional resources required to increase capacity

The BBN reported a range of resources required to increase capacity. These included:

1. Admin/technician time for registrations (Answering queries).
2. Admin time (arrange donations)

3. Transport costs (Donated tissue, funeral)
4. Neuropathology support
5. Provision of mortuary services/resources
6. Technician time
7. Laboratory consumables and reagents for histological diagnosis
8. Nurse time
9. Data manager

The availability of mortuary services

Although not an issue in Scotland, the availability of mortuary services has been highlighted as a constraining factor and the BBN were asked to make suggestions as to how to increase their availability for DPUK Cohort brain donations. Currently, there is a lack of clear policy guidance and the NHS is not obliged to carry out Brain Banking related work. As research has become increasingly separated from clinical services, mortuary staff do not consider brain banking related tasks as part of their job and the system operates on the basis of goodwill. With the progressive closure of local mortuaries and the centralisation of services on individual sites covering many hospitals, mortuaries are facing increased pressures such as staff shortages. In particular, mortuary services are regularly 'stretched' at holiday times and as a result, donations are being declined due to a lack of capacity. Furthermore, although most mortuaries remain very helpful and accommodating, others do not have a research licence to remove brains, or are now unwilling to assist in donation process due to lack of time/staff. The following suggestions/comments were made:

- Dialogue with mortuary managers in order to provide adequate financial incentives for extension of working hours including clear service level agreements with NHS Trusts and mortuaries.
- Payment for mortuary services may help to legitimise requests from brain bank and realistic fee payment for out of hours working might be an inducement.
- Training (a list of 'willing and capable" mortuaries is already partially in existence).
- Engagement programme for mortuary staff increasing awareness of benefits of research.
- Sponsoring training programmes for mortuary staff.
- Funding a member of mortuary staff to key mortuaries around the country may improve the situation in future. Given the unpredictable nature of the work, although the post could not be totally dedicated to brain banking, the general contribution to mortuary staffing would give legitimacy to the demands we place on them.
- DPUK consultation with mortuary managers regarding current situation and possible identification of better equipped &/or more willing mortuaries to inform strategic donor. However, transporting donors greater distances to

mortuaries will impact on post-mortem delay and will have significant cost implications.

- Even if mortuaries are available for longer hours both in the morning or evening the other constraint would be in obtaining the Medical Certificate of Cause of Death (MCCD) as donation cannot happen without it. Most GP's do not class viewing the deceased and writing the MCCD as a priority in their work load.

A remote registration and consenting process

Given the potential for large numbers of cohort participants to be offered brain donation through DPUK, one possibility under consideration is for the registration and consenting process to be managed remotely either by the Cohorts or through a participant resource centre. The BBN were asked to consider this possibility in relation to i) handling and storing consents, ii) answering participant queries, iii) co-ordination of brain retrieval, and iv) storage and distribution. The majority of brain banks highlighted that any increase beyond current capacity would require additional staffing and resources in relation to each of these areas.

i) Handling and storing consents

- Obtaining informed consent complex and requires specialist training.
- Training remote staff to HTA and ethics committees' standards would be difficult and could potentially result in multiple follow-up contacts to resolve inaccuracies/ inconsistencies /concerns.
- Additional DPUK Cohort specific training for brain bank research nurses may be required.
- Additional resources required by BBN staff to check consent forms and to process data.
- Physical storage for high volumes of paper documentation required but currently restricted across network with just 1 Brain Bank reporting that it would be possible to extend current processes and rely on current capacity to store consent forms locally.
- Suggestions
  - To maximise retention, initial general approach followed by specialist input for actual consenting.
  - Explore ethics of self-consenting via the web - electronic consenting for large numbers could be relatively straight forward in terms of storage and access.

ii) Answering participant queries

- Reduced burden on banks (Average query approx. 15-30 minutes plus variable amount of time for follow-up calls, depending on the nature of any subsequent questions).
- Potentially helpful for a central resource to manage contacts from families, GP's, nursing home, funeral directors etc. to enquire or clarify procedures at time of death or more specific questions about research.
- Provision of out-of-hours and holiday cover.

- A website based FAQ could be used
- Training of PI/staff of relevant cohorts required
- Potentially a massive burden if cohorts send out information to large numbers of participants and brain banks expected to field resulting queries.
- Similar systems currently in place for some cohort groups, but banks still receive a large number of enquiries directly.

iii) Co-ordination of brain retrieval

- Length of co-ordination process: Estimates included an average half a day of manager and nurse time and between 30 minutes and a whole day of phone calls to co-ordinate and organise all the different aspects depending on complexity and circumstances.
- Any additional donations – especially from outside local area – would have staff and time implications.
- Conversations with next of kin can be very time consuming
- Increasing numbers risks loss of goodwill and co-operation of mortuary staff which will impact on donations from existing prospectively assessed cohorts for which there is a clear tissue research plan and which should remain our priority.
- Scottish law does not recognise pre-mortem consent from a donor without capacity (i.e. signed by a power of attorney) and EBB would require a NHS Scotland post mortem request from to be completed after death before any retrieval can be undertaken. This requires a medically qualified person (GP, hospice doctor, senior research nurse), to explain the procedure and get consent from the appropriate relative or power of attorney post mortem.
- Suggestions:
    - A system could be developed using existing contacts with a national funeral director, requiring additional costs for national transport retrieval and timing would be dependent on neuropathology availability (EBB).
    - 1 Brain Bank suggested that there is great capacity for expanding their service based on extra funding for mortuary, transport costs and staffing (Tissue coordinator). (OBB)

iv) Storage and distribution

- With the majority of banks at capacity, funding would be required for additional transport costs, staff time, floor space, storage, equipment (e.g. freezers, racking systems for storing fixed specimens) and servicing to enable adequate storage for an increased number of donations.
- Volume and complexity of tissue requests will determine staffing needs.
- In some banks, storage space available but only accessible with the disposal of other wet tissue which implies additional staff time.
- Some banks reporting an increasing number of complex and large requests.
- Any planned targets for tissue supply time would also need to be considered and will likely require additional resourcing.

- In some banks, storage capacity built for the next few years based on current projections (e.g. 120 brains per year) and any change to this would have implications for space which would not be easily solved
- 1 Brain Bank suggested that assuming additional freezer space, the infrastructure and expertise exists for both storage and distribution (EBB)
- 1 Brain Bank provided the following costings for brain retrieval, storage and distribution

Approx. costings per donation	**Cambridge**
Co-ordination of brain retrieval	
Mortuary	£100
Transport (Donor to mortuary)	£180
Transport (Tissue courier to and from mortuary)	£90
Admin	£40
Storage and distribution	
Brain Dissection with consumables	£175
Storage	£160
Distribution per frozen/paraffin sample	£25
Admin	£40

Diagnosis

The BBN were asked to comment on the suitability of the 'BDR neuropathology SOP' for the diagnosis of the DPUK Cohort. Observations included:

- For donated tissue to be of use, it needs to be handled and diagnosed using the same protocol as other donations to the brain banks. The BDR SOP is already standardised across the BDR banks and would provide a good basis for this.
- Suitable but not for all donors. Alternative ways of neuropathology diagnostic work need to be explored and developed.
- Appears adequate for the purposes of the document but does not fully match the current processes of the Brain Bank (QSBB, SWBB)
- Sampling protocols could be accommodated
- Brain donation within 24 hours is usually very difficult (death over the weekend/MCCD not available until the next day, NOK /undertaker cannot bring deceased to the mortuary that day)
- MRC UK Brain Bank Network is developing diagnostic and clinical coding systems and these will be used. The BDR approach is overly simplistic.

Sampling Brain Tissue

Given the large number of DPUK Cohort participants, one strategy could be to store selected sample regions rather than the whole brain for these participants. The BBN were asked to consider whether this would be an effective and robust approach. Overall, the majority of comments from the banks supported the collection of whole brains. Reasons included:

- Sampling reduces storage costs in the long term but reduces sample availability and has no effect on the workload in terms of consenting or on infrastructure necessary for removing, processing and diagnosing donated cases or retrieving samples.
- If DPUK Cohort participants are valuable cases for research, after the expense and effort of organising additional donations, they should be utilised to their fullest extent and the maximum amount of tissue should be preserved. Additional storage space would be required, but the cost of this would be considerably less than the time and investment placed in following and finally securing the donations.
- Sampling greatly increases the chance of misdiagnosis.
- While it is possible to provide diagnostic information with around 90% reliability/accuracy through sampling 4 brain regions and employing 4 immunostains, evident that many other brain regions requested and solely storing blocks from these regions would severely limit the utility of the banked tissue.
- Sampling and storage from around 14 key regions (cf BDR protocol) increases flexibility.
- To future proof the project, whole brain storage a more sensible approach. Progress in research tools and knowledge implies that tissue samples from all brain regions may be requested for cases as old as 30 years. Availability of whole brain very important to ensure that research can be undertaken in the future. E.g. Localised DNA expression assessment.
- Disposal of most of the tissue donated 'simply' to limit storage issues seems 'morally wrong', and may ultimately restrict the value of the resource through future lack of availability of samples when initial samples have been used up, or were not taken in the first place.

Comments in support of sampling included:

- A prospective study will be required
- Yes, if a broad range of areas are sampled. Areas not identified as relevant to dementia diagnosis and research currently may become so in the future e.g. ALS example – C90rf72 pathology found in the cerebellum.
- Just storing paraffin blocks will help save space as retaining the whole brain requires a lot of room and storage facilities with good ventilation.
- Doubt about how useful tissue is for research when it has been fixed in formalin for a prolonged time.
- 1 Brain Bank does not store any whole brains currently, only pre-defined anatomical samples, and this works very well.
- If selected sampling is agreed as an option the rationale would need to be carefully thought out and the reasons clearly explained to participants

Tissue Requests

In the absence of an estimate of the number and the size of additional tissue requests that would be generated by the DPUK Cohort, discussing the implications and staffing

requirements is problematic. However, the BBN highlighted the significant amount of administrative and technical time required to handle tissue requests and as the current volume of tissue requests is already near capacity, additional technical staffing levels would be required. Co-ordinating data from multiple studies into an accessible and useful form whereby data is easily linked to relevant samples is complex and explicitly defined, collaborative operating procedures required between the banks and DPUK. The BBN raised the following aspects for consideration:

- Delegation of roles and activities for DPUK and the banks.
- Custodianship of tissue
- Tissue Request and Approval process,
- Timescale for completion of tissue requests
- Whether banks release tissue under their institution's existing Material Transfer Agreements (MTA) and tissue bank ethics. If so, applicants may have to face individual approval processes and complete up to 10 different MTAs in order to access tissue held in different banks.
- Whether tissue is subject to cost recovery &, if not, would DPUK reimburse these costs (particularly as any cost recovery resulting from the provision of tissue samples to researchers would take many years to accrue).
- Will tissue acquired via the DPUK Cohort be available to meet all bank requests or will banks be more of a storage solution for DPUK?
- Data access and data return management
- DPUK resource to be publicised separately or as part of MRC the main brain bank resources database?

Single site storage for DPUK samples

The banks were asked to consider the advantages and disadvantages of single versus multi-site storage for the DPUK Cohort.

<u>Advantages included:</u>

- Ok for small frozen samples (e.g. Milton Keynes Biorepository)
- Consistent and state of the art infrastructure
- Meeting tissue requests less costly and easier to co-ordinate
- Large amount of samples available on one site and providing 1 point of access for researchers.
- Remove additional pressure on local storage facilities
- Cost effective if only 1 centre has to resource staff, computer systems and storage infrastructure
- Centralisation collection makes it easier to control, catalogue, co-ordinate and to retrieve and process tissue for research.
- Centralisation could be effective assuming
- Adequate funding

- Consistency for labelling, consumables (e.g. frozen vial) and sample size to optimise storage capacities and traceability.
- Tissue requests met in a timely fashion
- Robust retrieval and courier processes and co-ordination to optimise transportation to DPUK centre

Disadvantages included:

- If whole brain, it would be difficult to access and fulfil requests
- As infrastructure already in place would be a more expensive option
- Geographical location crucial, impacting on PM delay and limiting how fresh tissue could be transported to the facility
- Reduces the local brain bank to the role of technician which would not be a positive approach
- Transferring samples from one site to another is expensive and time consuming. Practically difficult and expensive to operate due to brain transportation costs from donation to central storage site.
- Separation of samples and data
- If linked to 1 bank implies huge workload – for both diagnosis, maintenance of collection and processing of requests.
- Requires own facilities to sample brains and dispatch tissue requests independently without involving bank. Would also require neuropathological input for diagnosis.
- Currently, tissue request for BDR managed by co-ordinating centre and met from single or multiple sites depending on volume and complexity. Visibility of cases not a problem.
- Loss of samples by fire, power failure etc.

The possibility of DPUK registering as a new tissue bank modelled on the existing Brain Bank format was also considered by some banks. This would be based on a single site, could manage all aspects of the DPUK donation process. Benefits of this included i) a dedicated team for potential donors and donations, ii) Clear processes and control over the number of registrations, iii) No limits imposed by current infrastructure and storage capacity of the existing banks, iv) A dedicated mortuary service and no risk to the relationship between mortuaries and brain banks.

The effect of DPUK on the future sustainability of Brain Banking

Comments included:

- DPUK represents a huge opportunity for UK brain science, but careful discussion required in relation to i) expected scientific outcomes/value and ii) Funding.
- Uncertainty about the numbers and nature of DPUK participants each brain bank would be expected to manage makes projections problematic and too early to judge given issue requiring further clarification.
- Current structure will not cope with additional high volume of brain donation proposed.

- Reliance upon local Brain Banks implies major infrastructural costs and significant investment required to enable the banks to operate efficiently and to fuel high quality research.
- Longer term funding of DPUK a critical issue.
- Prioritising DPUK donations over current registrations raises strong concerns regarding declining donations, both in terms of staff emotional support and potential adverse publicity.
- A robust protocol for declining donations needs to be in place in case capacity is reached.
- Minimally invasive autopsies should be discussed for some participants (Olaf Ansorge is preparing a document on this matter following discussion with Simon Lovestone and Jacqui Oakley).
- With the increasing burden of dementia over coming decades and DPUKs commitment to recruit thousands of brain donors, the role of brain banks will become more important.
- Potential to increase patient and public engagement of donation process
- Increased public awareness of brain banking may lead to greater support from public and government.
- May help to standardise practices, ensure that well annotated material released in a timely fashion and increase size of tissue collections.

Section 3: A Brain Donation Strategy for DPUK

A protocol for a brain donation pilot study with UK Biobank was proposed by the DPUK Executive. This included 1) A pilot study linked to the intensive scanning of UK Biobank participants in the Manchester area, 2) A remote consenting process handled by the Participant Resource Centre at Cardiff University (the costs of which would be covered by UK Biobank) and 3) Brains to be stored by Manchester Brain Bank. The key stages of the pilot study are described in Figure 1 below.

NB At this stage no costings have currently been assigned by DPUK

The proposal was reviewed by three members of the BBN: Professor Seth Love (Director), Dr. Olaf Ansorge (Neuropathologist, Oxford Brain Bank) and Dr. Jacqui Oakley (MRC Programme Manager for Neurosciences and Mental Health). The summary below provides responses to the proposal and makes recommendations for a long term DPUK brain donation strategy. Individual responses are provided in Appendix 1.

<u>Responses to the proposal</u>

1. A reasonable protocol for a pilot study
2. Given a lack of available capacity in Manchester brain bank, prior to commencement of the pilot, consultation with the bank is required to agree
    - Additional cost coverage (e.g. funding per consent/brain, total number of brains over a fixed period)
    - PRC training
    - Data shared between bank & UK Biobank
3. As a starting point for estimating the financial impact of the pilot study, further information needs to be supplied in relation to
    - Number of participants to be approached for brain donation & likely level of participant uptake (Pending the results of a UK Biobank survey of interest in brain donation)
    - Characteristics of participants selected for brain donation (e.g. sociodemographic data, geographical location, morbidity)
4. A link with UK BioCentre could be considered if storage is a problem

<u>Recommendations for a long term DPUK brain donation strategy</u>

1. A decentralised model based upon the accommodation of extra DPUK activity within existing brain bank infrastructure across the 10 brain banks
    - A relatively modest investment to cover increased marginal costs
    - Allows for local collection of brains *with minimal transportation*
    - If approach based solely on Manchester Brain Bank, aligning sampling protocols may be more difficult.
    - A shift away from ad hoc donation may free up capacity

2. Disassociation of timing and geographical distribution of additional scanning of UK Biobank participants with consent for brain donation.
    - Inclusion of geographical location in MRI selection criteria to facilitate distribution of registration and brain donation across banks according to capacity and over 5 years
    - Leading to more effective planning to meet implied future substantial cost increases (e.g. staffing, neuropathology, consumable costs, storage)

3. Formulation of DPUK brain donation strategy dependent upon
    - Clarification of scientific questions, definition of brain donation subgroups and criteria employed (Identification of discussion lead)
    - Identification of what we want to learn from the donated brains.
    - Number of participants to be approached for brain donation & level of participant uptake
    - Characteristics of cohorts selected for brain donation (e.g. sociodemographic data, morbidity)
    - Prioritisation and criteria for accepting DPUK brains
    - Anticipated number of additional tissue requests arising from DPUK banked tissue (Linked with actuarial analysis)
    - Timeline for the updates to the SOP for brain collection

4. Actuarial analysis key to informing the anticipated impact of UK Biobank deaths in terms of updating/reassuring brain banks, identifying the best way to accommodate donations and scheduling necessary resource increases.

5. Driven by scientific questions, DPUK represents an opportunity to develop innovative approaches (e.g. providing raw histology data to DPUK in form of digital images for quantitative trait analyses) and to orchestrate different types of brain donations including 1) Full post-mortem with brain, cord and systemic tissues, 2) Full brain (frozen / fixed) and 3) Limited sampling (e.g. frozen and FFPE blocking with no residual wet tissue).

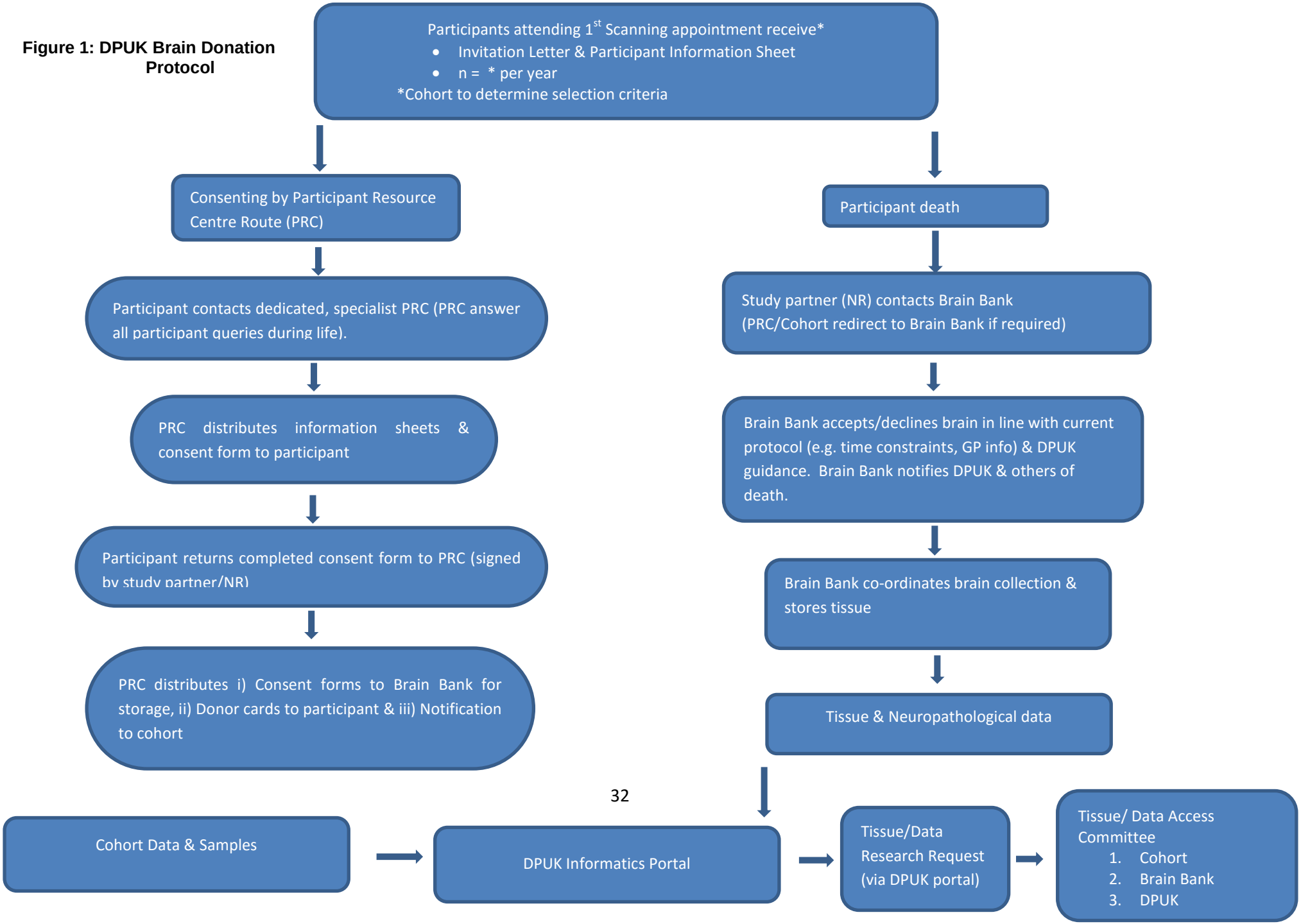
6. A model based on remote consenting would allow for the consolidation of consenting expertise specific to DPUK cohorts related issues and would minimise impact on the banks themselves. Collection across the 10 banks would relieve the busiest banks and address highlighted capacity issues but aligning sampling protocols may be more difficult.
    - Findings of the pilot study, if based on PRC consenting, will inform further discussion.

7. Given capacity constraints, the option of central collection and storage should be explored
    - This approach may be more appropriate for certain cohorts or subgroups of samples.

- UK BioCentre in Milton Keynes, commissioned via Oxford University, is the obvious central collection point as this is going to handle samples and data from both GEL and UK Biobank. Further advantages include the provision of DNA, RNA extraction and quality control at scale. Dr. Olaf Ansorge able to provide feedback on a centre briefing to the MRC Network Meeting if appropriate.
- Selecting a small number of specialised centres for collection and storage would allow stand-by banks to be utilised if any one bank is not able to accommodate a collection.

8. Investment required for enhancing integration of brain bank and UK Biobank IT systems to facilitate bidirectional information transfer

Figure 1: DPUK Brain Donation Protocol



Appendix 1: UK Brain Bank Questionnaire

Assessing the Current Capacity of UK Brain Banks

The primary aim of Work Package 13 is to assess the feasibility of offering brain donation to the DPUK Cohorts. Evaluating the capacity of the brain banks and documenting the current workload of the brain banks is therefore an essential step in understanding the implications of the Work Package for brain banking practice.

The information provided by the Brain Banks will form the basis of a Brain Banking Strategy Report which will outline key strategic decisions, proposals and resource implications relating to the extension of brain donation to DPUK Cohorts. Following circulation within the MRC UKBBN, the report will be submitted to the DPUK Executive.

Thank you for completing this questionnaire. Please return to helen.costello@kcl.ac.uk by

Friday 3rd July

Brain Bank:

Completed by: *(Name & role)*

Section 1: Current Capacity

1. Between 01/01/14 & 31/12/14, please specify the number of control/healthy brains collected.

2. Between 01/01/14 & 31/12/14, please specify the number of diseased brains collected (Including diagnosis).

3. Of the total brains processed between 01/01/14 & 31/12/14, please specify the proportion of brains from

   a. Cohort studies (Please specify)

   b. From registers (Please specify)

   c. Ad hoc donations

4. Does the brain bank have any ongoing commitments to any particular Cohorts? If so, please describe

5. Has the proportion of brains collected from Cohorts, registers & ad hoc donations changed in the past 3 years? If so, please describe how & why you think this is the case.

6. Referring to the ***'Service Support Costs for 2015 in the MRC UK Brain Bank Network'*** (attached), what if any, additional resources are required by the Brain Bank? (e.g additional technicians, post-doc time, mortuary services, data management, admin. time)

7. Please describe current staffing levels of the Brain Bank in terms of job title & FTE (Include manager, technicians etc.)

8. Please estimate the workload (in terms of staff & hours) to manage 10 new donor registrations.

9. Assuming current practices and the current level of resources, is the Brain Bank currently in a position to process an increased number of brains?

    a. If yes, how many per month?

    b. If no, please describe the prohibiting factors?

10. How many brains does the bank currently store? Please specify nature & method of storage.

11. Does the brain bank currently have any unused/additional storage? If so, please specify nature & amount of storage (e.g. room temperature, freezer).

Section 2: Collecting Clinical Information & Declining Donations

1. Before a decision to proceed to brain donation is made, does the Brain Bank collect any clinical information? Please specify type of information and method of collection. (e.g. retrospective interview with family, medical records)

2. What criteria does the Brain Bank use to determine whether to accept a brain?

3. Please estimate the number of brains currently declined between 01/01/14 & 31/12/14.

    a. Is this number expected to increase? If so, why?

4. Please describe most common reasons for declining donations

5. What is the process for declining donations (e.g. who does the declining, length of time typically required to talk to relatives etc.)

Section 3: Extending Brain Donation to DPUK Cohorts

While it is not yet possible to be precise about the number of Cohort participants expected to consent through DPUK, it is possible that approximately 10,000 individuals could be approached through UK Biobank over the next 5 years. One possibility is that the consenting process will be co-ordinated by DPUK and/or Cohorts PIs, whereby information and consent forms providing Brain Bank contact details (including procedures for reporting deaths) are distributed by DPUK and/or Cohorts PIs.

Please describe the implications and additional resources that you feel would be required to facilitate this in relation to:

a. Handling & storing consents

b. Answering participant queries

c. Co-ordination of brain retrieval

d. Storage & distribution

e. Any other issues

2. Please describe any issues that you think may arise from handling tissue requests for the DPUK Cohort (e.g volume of requests, access to data)

3. For the diagnosis of DPUK Cohorts, would the **'BDR neuropathology SOP v1 22052015'** (attached) be acceptable? For example, is there anything else that you would like to see added/removed? Please describe.

4. The availability of mortuary services has been highlighted as a constraining factor; do you have any suggestions as to how to ensure that mortuary services are made available for brain donations from the DPUK Cohort?

5. Given the large number of DPUK Cohort participants, one strategy could be to store selected sample regions rather than the whole brain for these participants? Do you think that this could be an effective and robust approach? Please give reasons.

6. Given the large number of DPUK Cohorts, one strategy could be to store DPUK samples on a single site. What do you perceive to be the advantages and disadvantages of this approach?

7. How do you think that DPUK will affect the future sustainability of the Brain Banks?

THANK YOU FOR COMPLETING THE QUESTIONNAIRE

Appendix 2: Summary of capacity report & responses to proposed brain donation study pilot protocol

Professor Seth Love: Director MRC Brain Bank Network

25-07-15

A huge challenge to try to devise a one-size-fits-all centralised solution for registration, consenting and subsequent communication relating to all DPUK brain donations across the UK, even if a lot of money were spent on extra staff and additional training, whereas it would require a more modest investment to cover the increase in the marginal costs of accommodating the extra activity within the existing brain bank infrastructure.

I suggest that one aspect of the solution is to dissociate the timing and geographical distribution of the approach for donor registration from those for the recruitment for MRI scanning etc. I presume the important thing is simply that the two processes eventually converge (i.e. the same 10,000 people who have the additional scans and cognitive tests are eventually also consented for brain donation). This will require planning and coordination but should be simpler and less expensive to implement than trying to do everything at the same time. There will certainly be some extra costs, and they should not be ignored. However, the up-front costs should be modest; the more substantial costs, for brain bank staffing (including neuropathology staff), freezer space won't be incurred for some years, which gives us time to devise ways of covering them.

One expense that I don't think should be avoided is investment in better integration of the brain bank and UK Biobank IT systems to facilitate the passage of information relating to DPUK donors to and from the brain banks. We've been making excellent progress in increasing the functionality of the MRC brain bank database but this is not supported by any DPUK money (which will simply fund equipment for bar coding and sample tracking), and the MRC brain bank database is simply a repository of information uploaded from the individual brain banks not a means of bidirectional information transfer.

15-09-15

As indicated previously, my preferred solution would be to cover the increase in the marginal costs of accommodating the extra activity within the existing brain bank infrastructure by (i) deciding on the MRI selection criteria for UK Biobank participants - and those criteria should include geographical spread, (ii) seeing which UK Biobank participants across the whole of the cohort meet those criteria, (iii) allocating those participants to the nearest brain bank, and (iv) spreading the process of contacting and registering the relevant UK Biobank participants for brain donation over several years.

I think it would be reasonable to evaluate the centralised approach outlined in Section 3 in this pilot study. However, any decision on whether to proceed with the pilot study should definitely be preceded by consultation with Manchester brain bank. I'd also note that the brain bank needs to have (and have logged into its system) all of the relevant paperwork and contact details (for the GP, nursing home/care home, family, GP, local mortuary, local undertakers and local coroner) in advance and should be contacted immediately after

the prospective donor has died to ensure that the brain bank has all of the correct paperwork, that the death certificate has been issued (unless the coroner is involved), and to make the necessary arrangements with the GP, mortuary, undertakers and sometimes the local coroner for the donation to take place within a reasonably short time after death. Otherwise, these could end up in the same category as ad hoc donations, which cause major logistical problems are which have a much lower success rate than planned donations. Sending out information sheets and consent forms is the easy bit!

Dr. Jacqui Oakley: Programme Manager for Neurosciences and Mental Health Medical Research Council

The actuarial analysis within this work package will be key to informing us of the anticipated impact of UK Biobank deaths. This will a) help us to plan the best way to accommodate these donations and at which point we might need to ramp-up resources b) update and reassure banks of the anticipated impact.

The report highlights that, at present there are large differences in the proportion of ad hoc vs registered brains being collected between the banks.

Possible models:

- Decentralised consenting, collection and storage centres where brains are collected across the 10 banks in the Network and donors being consented at their local bank (impact on each bank ?).

This model would allow for the local collection of brains with minimal transportation. If the participants invited for rescanning are based in Stockport alone, this may be a less favourable model. This model may make it more difficult to align sampling protocols.

- Centralised consenting centre with decentralised collection and storage across the 10 banks.

This model would allow for consolidation of consenting expertise specific to DPUK cohorts related issues, with less impact on the 10 brain banks themselves. Collection across the 10 banks would relieve the busiest banks and address some of the capacity issues highlighted as concerns. Again, this model may make it more difficult to align sampling protocols.

- Centralised consenting and collection centre with a selection of specialised centres for tissue collection and storage.

This model would allow for consolidation of consenting expertise specific to DPUK, with
less impact on the 10 brain banks themselves. Selecting a small number of specialised centres for collection and storage would allow stand-by banks to be utilised if any one bank could not accommodate a collection.

<u>Outstanding queries</u>

- Are there plans to prioritise the 10, 000 consented donors for donation or will we take them all?
- What is the anticipated number of additional tissue requests arising from DPUK banked tissue. This will link in with the actuarial analysis.
- What is the timeline for the updates to the SOP for brain collection?

Dr. Olaf Ansorge: Lead Neuropathologist, Thomas Willis Oxford Brain Collection

Background

The aims for DPUK state 'sustainable tissue donation' of up to 10,000 brains from DPUK cohorts. My understanding is that this is in addition to any donation pledges from existing cohorts (e.g. BDR). It is further stated (Paper 3, MRC DPUK Overview) that any DPUK protocols must allow 'for brains to only be recovered if scientifically informative'. WP13 of DPUK was set up to explore how such a donor programme could be run, and whether it could be accommodated by the existing MRC Brain Bank network.

Outcome

The WP13 capacity report provides a good overview of the UK brain banking landscape. There is evidence of harmonisation across subgroups of banks (BDR, MRC); however, striking variations exist in the estimated workload for managing new donations (table 10). This makes it very difficult to estimate the potential financial impact of additional donations from DPUK cohorts. The discrepancy may partly be due to lack of clarity of the definition of terms. The data is also incomplete. However, it seems clear from the survey that there is currently little spare capacity.

Comments

1. I have studied the DPUK platform documents on the web and also those that Jacqui made available to me (from which I quoted above). However, I cannot find information on (a) which cohorts should be specifically targeted for brain donation and (b) what the scientific questions are. I appreciate that this may emerge at a later stage and also change after participants have been invited to consider brain donation. It seems that many more than 10,000 participants will be invited, but only up to 10,000 brains collected (?). Will only those that are scanned be invited?

No estimate of the impact on existing brain bank infrastructure can be made if we do not know which cohorts are considered priority for brain donation, how they are geographically distributed, and what the projected life expectancy is. This needs to be decided and modelled: Who is going to lead the discussion on defining the brain donation subgroups, and what are the criteria?

Linked to this is of course the question of what we want to learn from the donated brains. My impression (from Simon Lovestone) is that we as neuropathologists have an opportunity to shape this to a large degree, and that the expectation is to come up with some innovative approaches (for example – provide raw histology data to DPUK in form of digital images for quantitative trait analyses).

We should consider that there may be different types of brain donations, for example: 1. Full post-mortem with brain, cord and systemic tissues; 2. Full brain (frozen / fixed); 3. Limited sampling (e.g. frozen and FFPE blocking with no residual wet tissue). Scientific questions should drive this.

2. Network vs. central collection and storage

I think the report gives a good overview of the pros and cons for each approach, and I agree that the main aim should be to map DPUK donors on existing infrastructure and ask for the marginal incremental costs. However, given that the report suggests most centres are working at capacity, the option of central collection and storage should at least be explored further - it may be relevant for certain cohorts or subgroups of samples?

The obvious central collection point would be the UK BioCentre in Milton Keynes, commissioned via Oxford University, as this is going to handle samples and data from both GEL and UK Biobank. I am going to attend a briefing on the centre in the next couple of weeks and would be happy to report back to the November MRC Network Meeting (please let me know if this would be of interest). One selling point of the centre is that it would also provide DNA, RNA extraction and quality control at scale, for example.

3. Pilot UK Biobank study with central consenting – Manchester

This should go ahead but of course Manchester need to be consulted. If storage is a problem, a link with UK BioCentre should at least be considered.