Cognitive Assessment
Work Package 10

Objectives:

To build on UK Biobank cognitive testing infrastructure and deliver additional cognitive phenotyping in 100,000 participants with concurrent 3T MRI.

1. **Enhance the UKB cognitive battery**: by the addition of tests for crystallised intelligence and executive function. The addition of cognitive testing to this cohort would enable it to become a dedicated dementia research cohort.
2. Provide **repeat cognitive assessment at repeat imaging**: recruited for repeat brain imaging at 24 months follow-up.
3. **Recruitment of informants**: Informants (carers, family members), can be highly valuable sources of information in situations where participants are suffering significant cognitive decline who potentially could be lost to cognitive follow-up
4. **Calibration and psychometrics of cognitive assessment**: The programme aimed to fully describe and explore the psychometric properties of the available cognitive data. An additional component of the calibration studies should be to validate the enhanced cognitive test battery against well-known and well-validated cognitive tests.
5. **Identification of dementia syndromes**: Investigation of the feasibility of cognitive testing strategies for distinguishing between cognitive syndromes such as AD, frontotemporal lobar degeneration and dementia with Lewy bodies in population studies.
6. **Contact and re-contact strategies**: Development of cost-effective contact and re-contact strategies.

Overview Summary:

The UK Biobank cohort of ~500,000 men and women (aged 40 to 73 years at baseline) was repurposed as a dementia-focused research resource by developing an enhanced cognitive test battery for follow-up assessment. The group also created several resources for the community hosted on the DPUK web-site. This included a cohort cognitive test directory and details of key resource papers for cognitive research.

Executive Summary:

This Work Package repurposed the UK Biobank cohort as a dementia research resource by developing an enhanced cognitive test battery for assessing cognitive ageing trajectories in participants remaining in the study. The battery includes tests of processing speed, executive function, and episodic memory, which are cognitive domains that are sensitive to changes in healthy and pathological ageing. The work package conducted a psychometric analysis of the enhanced cognitive test battery, including a formal assessment of its test-retest reliability and concurrent validity. This was an Edinburgh-based study of 160 adults who completed the 11 UK Biobank tests alongside well-validated and standardised psychometric tests of equivalent cognitive domains. A subset of volunteers returned to repeat the UK Biobank tests after four weeks, to test short-term reliability.

The group further advised UK Biobank in the ongoing assessment of cognitive function, including issuing reports on recruitment of informants, reporting on subjective memory complaints, and, site-visit observations on the reliability of the enhanced cognitive battery.

Results

UK Biobank has implemented the enhanced cognitive battery at the imaging assessment (target: n=90,000) with current data on >32,800 participants (as advertised on UK Biobank Data Showcase on 3rd March 2020). In the validation study of the enhanced battery, most tests showed modest to good concurrent validity when compared to well-validated tests thought to measure the same cognitive domains.

Psychometric properties of all UK Biobank's cognitive tests have been written up as a report for researchers. Other key resources for cognitive ageing research cover advice on cognitive testing measures and a cognitive testing directory of all DPUK's existing cohort studies (n = 39).

UK Biobank have not yet instigated recruitment of informants, nor administration of subjective memory questionnaires. It ruled out telephone assessments for cost reasons.

Several epidemiological publications from this group focus on cognitive data in UK Biobank.

Summary of Outputs: (By Researchfish categories)

Five most important publications

- **Calvin CM, et al. (2017) Childhood intelligence in relation to major causes of death in 68 year follow-up: prospective population study. *BMJ*, 357:j2708. doi: https://doi.org/10.1136/bmj.j2708**

Evidence from this whole population birth cohort study linking childhood intelligence test scores to causes of death, in a follow-up period spanning ages 11 to 79 years, demonstrated how this childhood trait is associated with lifetime risk of dementia-related mortality, with a stronger effect in women relative to men. This highlights the importance of considering a lifespan approach to studying dementia risk and to developing intervention strategies.

- **Calvin CM, et al. Predicting incident dementia 3-8 years after brief cognitive tests in the UK Biobank prospective study of 500,000 people. *Alzheimer's and Dementia*; *The Journal of the Alzheimer's Association*, 15(12), 1546-1557. doi: https://doi.org/10.1016/j.jalz.2019.07.014**

This observational study demonstrated an association between preclinical cognitive capability in adulthood and risk of incident dementia ascertained through data linkage to routine electronic health records, thereby avoiding the issue of attrition common to previous studies. It accounted for a range of constitutional, genetic and modifiable risk factors for dementia, and found evidence that brief cognitive testing could be a valuable addition to population screening for dementia risk.

- **Cox SR, et al (2019). Associations between vascular risk factors and brain MRI indices in UK Biobank. *European Heart Journal*, 40(28), 2290-2300. doi: https://doi.org/10.1093/eurheartj/ehz100**

Using data from 9722 Biobank participants, aged 44-79 years, the authors studied the association between multiple vascular risk factors (VRF) and brain micro/macrostructure. The effect sizes were small, but higher levels of VRFs were associated with poorer grey and white macrostructure and microstructure and the effects were additive. The brain areas most strongly affected were those previously linked with 'typical' Alzheimer's Disease, and with more complex cognitive

functions. These results suggest that even in otherwise healthy participants, and even in middle age, the brain is vulnerable to VRFs, and that cognitive decline could be partly ameliorated by addressing malleable VRFs.

- **Cox SR, et al. (2019). Structural brain imaging correlates of general intelligence in UK Biobank. Intelligence, 76, 101376. doi: https://doi.org/10.1016/j.intell.2019.101376**

Using data from the UK Biobank imaging study, this paper examined the brain imaging correlates of general intelligence (overall n = 29,004; n for participants providing MRI and scores on all four cognitive tests of interest = 7,318). A general factor of intelligence was created using four of the UK Biobank cognitive tests. In this study, larger total brain volume was associated with higher intelligence. This is one of the largest studies of the association between brain size and intelligence.

- **Fawns-Ritchie C, Deary IJ. Reliability and validity of the UK Biobank cognitive tests. [Submitted for peer-review. Preprint at *Medrxiv.org:* https://doi.org/10.1101/19002204]**

This study investigated the concurrent validity and short-term test-retest reliability of the full UK Biobank cognitive test battery. A sample of 160 participants (mean age=62.59, SD=10.24) completed the UK Biobank cognitive assessment and a range of well-validated cognitive tests, and 52 participants returned 4 weeks later to repeat the UK Biobank tests. The UK Biobank cognitive tests showed a range of correlations with corresponding well-validated tests, i.e. those tests that were thought to assess the same underlying cognitive ability (mean Pearson r=0.53, range=0.22 to 0.83, p≤.005). Four-week test-retest reliabilities of the UK Biobank tests were moderate-to-high (mean Pearson r=0.55, range=0.40 to 0.89, p≤.003). Despite the brief, non-standard nature of the UK Biobank cognitive tests, some showed substantial concurrent validity and test-retest reliability.

Other publications:

- Calvin CM, et al. (2019) Sex-specific moderation by lifestyle and psychosocial factors on the genetic contributions to adiposity in 112,151 individuals from UK Biobank. *Scientific Reports*; 9:363.
- Calvin CM, et al. (2017). Moderating lifestyle and psychosocial factors on genetic susceptibility to dementia comorbidities: An MRC Dementias Platform UK (DPUK)-supported study. *Alzheimer's and Dementia: The Journal of the Alzheimer's Association*; 13(7): P1179.
- Hagenaars, SP, et al. (2018). Genetic risk for neurodegenerative disorders, and its overlap with cognitive ability and physical function. *PLOS ONE*; *13*(6); p.e0198187

Collaborations & partnerships

Close working with UK Biobank.

Further Funding

Engagement Activities

Scientific talks and posters

- Calvin C. (2017). *Do cognitive test data in UK Biobank add to prediction of incident dementia?* Oral presentation at Dementias Platform UK Annual Conference, Royal College of Obstetricians and Gynaecologists, London on 4 May 2017.
- Calvin C. (2018). *Data portal workshop [included work of the cognitive assessment team in developing meta-data for the online researcher discovery tools]*. Oral presentation at Dementias Platform UK Annual Conference, British Medical Association, London on 23 April 2018.
- Calvin C, et al. (2018). *Cognitive measures in DPUK cohorts: A resource for researchers*. Poster presentation at Dementias Platform UK Annual Conference, British Medical Association, London on 23 April 2018.
- Calvin C, et al. (2018). *Predicting incident dementia from cognitive test performance in UK Biobank*. Poster presentation at Alzheimer's Research UK, QEII, London on 20–21 March 2018.
- Calvin C. (2019). *Cognitive test harmonization across Dementias Platform UK cohorts*. Oral presentation at International Data Harmonisation ESRC Workshop on Cognitive Ageing and Dementia: Perspectives from the UK and Japan, University College London on 8 November 2019.
- Fawns-Ritchie C. (2018). *Impact across the platform: Perspective of an ECR.* Oral presentation at Dementias Platform UK Annual Conference, British Medical Association, London on 23 April 2018.
- Fawns-Ritchie C, et al. (2017) *MRC Dementias Platform UK WP10: Examination of the psychometric properties of UK Biobank cognitive tests.* Poster at Dementias Platform UK Annual Conference, Royal College of Obstetricians and Gynaecologists, London on 4 May 2017.
- Fawns-Ritchie C, et al. (2018). *Psychometric evaluation the cognitive assessment in UK Biobank: Dementias Platform UK Cognitive Assessment*. Poster presentation at Alzheimer's Research UK, QEII, London on 20–21 March 2018.
- Fawns-Ritchie C, Starr JM, Deary IJ. *Preliminary psychometric results from the enhanced UK Biobank cognitive test battery: Dementias Platform UK Cognitive Assessment*. Poster presentation at Dementias Platform UK Annual Conference, British Medical Association, London on 23 April 2018.
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Influence of policy, practice, patients & the public

The group produced a series of internal reports for UK Biobank.

Research tools & methods

Cohort cognitive test directory (see DPUK website)
Summary of key resources for cognition research (see DPUK website)

Research Databases & Models

None

Intellectual property & licencing

None

Medical products, interventions & clinical trials

None

Artistic & creative products
None
Software & technical products
None
Spin outs
None
Awards & recognition
In the 2019 New Year Honours, Ian Deary was awarded an OBE for services to the Social Sciences.
Other outputs & knowledge/future steps
None
Next destinations
Chloe Fawns-Ritchie – Early Career Researcher Post-doctoral research assistant, Generation Scotland, University of Edinburgh Catherine Calvin – Early Career Researcher From 20 April 2020: Data Analyst, Nuffield Department of Population Health, University of Oxford
Use of facilities & resources
None
Most successful outcome and what it means for future dementia research:
Work Package 10 was successful in its initiative to repurpose UK Biobank as a dementia research resource, by developing an enhanced cognitive test battery for implementation at follow-up assessment of this cohort. The enhanced battery has so far been completed by over a third of the 90,000 participants who are being invited to return for imaging assessment. These accumulating data will be sensitive to between-person differences in cognitive function; and allow for the investigation of predictors and consequences of level of cognitive ability, and rate of cognitive decline in older adulthood. UK Biobank currently has over 100 approved studies with a dementia focus. Over time this cohort of half a million adults in mid-to-late adulthood will increasingly be relevant to dementia researchers worldwide, including a high demand for these detailed cognitive data.
Lessons learned:
Work Package researchers learned to work within certain constraints imposed by the UK Biobank team with its competing priorities and multiple scientific interests. This influenced the selection of cognitive tests for the enhanced test battery. In addition, after sending proposals to UK Biobank requesting the recruitment of informants and assessment of subjective memory, UK Biobank opted not to implement them for several reasons including the lack of procedures for obtaining informants. Accordingly, some of the original objectives were not met. This released some time for WP10 members to focus on other projects: 1) an investigation of the psychometric properties of the UK Biobank tests; 2) the creation of cognitive testing resources for the Dementias Platform UK website; 3) the undertaking of epidemiological studies utilising the cognitive data in DPUK's cohorts.
Other:
None