IMPACT

INNOVATIVE TOOLS FOR DEMENTIA DIAGNOSIS

DRC DEMENTIA RESEARCH CENTRE

EPSRC Pioneering research and skills

UCL

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Impact Objectives

- Generate multivariate cognitive profiles in different dementias
- Develop novel 'instruction-less' tests of cognition suitable for patients with different types and severities of dementia
- Enhance existing cognitive assessment paradigms using eye tracking

Innovative tools for dementia diagnosis

__Professor Sebastian Crutch__, __Dr Neil Oxtoby__ and __Emilie Brotherhood__ are part of a multidisciplinary team committed to applying the same computational approaches currently used on neuroimaging data, to the assessment of cognitive impairment

Professor Sebastian Crutch

Dr Neil Oxtoby

Emilie Brotherhood

Why is it important to improve tests for cognitive impairment when assessing patients who have or may be at risk of developing dementia?

SC: Cognitive impairment relates to changes in memory, perception, language, decision-making and other mental skills associated with different forms of degenerative brain disease. Dementia is generally defined as the point at which these changes start to interfere with everyday life. There are many different types of dementia and understanding the cognitive profile of each is critical to diagnosis, patient monitoring and evaluation of treatments. Many tests fail to capture critical, sensitive aspects of task performance such as naming tests which measure the accuracy with which someone can retrieve a word but miss other sensitive performance indications such as how long it takes to do so. The tools we currently have to assess cognition are important and valuable, but many have changed little in the past three or four decades and are often long to administer and tiring for people undergoing assessment. With the advent of a slew of computational approaches for analysing complex datasets, greater computational power and new tools for evaluating different aspects of human psychology and physiology, cognitive assessment is long overdue a step change in approach akin to the many advances in brain imaging we have seen in recent years. The C-PLACID project brings together clinicians and computer scientists to lay the foundations of such a change.

What types of testing do you advocate and in what way are these better than current methods?

SC: We aim to combine the principles of traditional tests with new technology and analytical methods. One example is our eye-tracking analysis of spatial anticipation in patients with frontotemporal dementia. Rather than merely focusing on the motor function of the eye, we are using eye motion as an indicator of anticipative cognitive ability. Our initial results indicate that the fine-grained, rich datasets obtained from eye-tracking measurements can inform us about high level cognitive functions in dementia. By using machine-learning we can identify conditions where subtle deficits are present and thereby contribute to test optimisation and the reduction of testing times. Such tests also avoid the need for instructing patients on how to complete the tasks, which rules out mistakes caused by misunderstandings or language difficulties.

What has the key to your project's success to date been?

NO: We have been able to blend and combine a number of different techniques and disciplines because we are in a rare position at UCL, with the co-location of researchers from many different fields. The project team sits at the interface between medical engineering and the clinic. Our success is based on the willingness of staff on both sides of that professional and experiential divide to immerse themselves in another world. For instance, our computer scientists are meeting people with different dementias and trying to understand their experiences, for example, at our regular support group meetings. Likewise, clinicians are embracing some of the principles and advantages offered by machine-learning.

What objectives has the project met so far?

EB: Our first goal was to develop multivariate computational models for all types and stages of different types of dementia. In this, the results have exceeded expectations and proven the potential of this type of machine-learning to predict the progression of disease, based on different events which signify notable changes in condition. The second set of goals is to improve cognitive tests using novel technologies such as automatically measuring voice reaction times and tracking eye movement in a spatial anticipation task. Over 850 people have undergone eye tracking and other tests are being implemented on 500 of the 1946 British-birth cohort during its second phase of neuropsychological testing. Other tasks are underway, including the use of virtual reality to assess ability to function in different social settings.

Machine learning applied to dementia

The __C-PLACID__ project represents a major push by different centres at __University College London__ to apply machine learning and new cognitive assessment tools to the diagnosis of dementia to improve patients' quality of life and inspire a new generation of researchers

The incidence of dementia increases in parallel with greater life expectancy. The World Health Organisation predicts that the number of people living with dementia worldwide will triple by 2050 and the Alzheimer's Disease Neuroimaging Initiative estimates that it is the third most common cause of death for elderly people in the US. Being able to diagnose different forms of dementia and to plot the evolution of disease is an important component of tackling this problem. Early and accurate diagnosis, which leads to better management and improved quality of life for patients, is the focus of the three-year C-PLACID project that is developing a sophisticated computational platform for the assessment of cognition.

The project has brought together researchers from many disciplines within University College London (UCL), including computer scientists, mathematicians, engineers, psychologists and dementia clinicians. Principal investigator, Professor Sebastian Crutch of the Dementia Research Centre at UCL, believes that: 'Cognitive assessment is long overdue a step change in conduct, precision and efficiency,' and adds: 'Many of today's tests fail to capture critical, sensitive aspects of task performance and can be long and tiring for the patient to undergo.' The project aims to create and validate event-based models for dementia, improve current tests and develop innovative cognitive assessment methods.

A scene from the virtual cafe bistro in which immersed participants observe and interact with avatars in different social scenarios

TESTING FOR COGNITIVE IMPAIRMENT

The term 'dementia' covers a range of conditions, including Alzheimer's disease, dementia with Lewy bodies, the visual syndrome posterior cortical atrophy, frontotemporal dementia, and vascular dementia. Patients are referred to a specialist once they notice signs of diminished memory, language, reasoning or other cognitive skills. In addition to potentially undergoing neuroimaging, people under assessment are commonly subjected to a battery of cognitive tests. However, Crutch explains that these tests have several limitations: 'Many of today's tests do not have the sensitivity to distinguish between different types of cognitive impairment and results can be affected by the ways in which each clinic carries out the assessment. Some require complicated instructions and there are domains of cognition that they cannot assess.'

It is vital to identify the specific condition and the stage of progression of a patient's disease. Pinpointing these markers with accuracy enables the development of a more specific prognosis and care plan. The C-PLACID project is bringing the same sophisticated analytical techniques into the realm of cognitive assessment that are already applied to the interpretation of neuroimaging data. Crutch explains: 'As well as developing a computational platform for the analysis and visualisation of complex cognitive datasets, we are automating, optimising and creating techniques and devices for the acquisition of traditional and new cognitive data.' The project will provide solutions to the many problems of assessment that have been highlighted by clinicians and develop tests that do not require instructions. The results are intended to benefit both clinicians and patients, with the latter benefiting from shorter, less stressful testing and better management of their specific condition.

EYE TRACKING AND VIRTUAL REALITY

One of the innovative testing techniques being developed by the team is the design of instructionless eye-tracking tests of cognition. In one experiment, patients with different forms of dementia are given a computerised version of the Brixton spatial anticipation test. This test shows patients a matrix of white circles through which a black dot traces patterns that are followed by the eye, with the pattern changing unpredictably. Patients are normally required to give a verbal indication as to where the dot will appear, whereas in the computerised version, the eye motion is automatically tracked. Trials were conducted on 12 behavioural variant

Cognitive assessment is long overdue a step change in conduct, precision and efficiency

frontotemporal dementia patients (bvFTD) who were expected to show deficits in this test; six semantic dementia patients who were expected to show less impairment in undertaking this task and 38 healthy controls. The eye movement measurements were studied using both frequentist statistical analysis and machine-learning algorithms trained on healthy datasets. The machine-learning approach performed far better than both the original pen and paper testing of the same patients and the results from the frequentist statistical analysis. Crutch says: 'It reported significant differences from controls in all the trials conducted on bvFTD patients and in half of the SD patients, whereas both other approaches missed deficits in a significant proportion of participants.'

A number of other novel testing techniques are being developed and tested by the team. Mark Huckvale, a speech scientist from UCL, has helped create a means to complement picture-naming tests with measures of response speed. 500 members of the 1946 British-birth cohort are currently undergoing this test to determine if naming speed is indicative of the build-up of proteins in the brain associated with Alzheimer's disease. There are ethical and privacy considerations to be considered, but the trial showed that important cognitive data can be mined from the way the patient engages with the device.

Emilie Brotherhood, a research scientist at the UCL Dementia Research Centre, has been involved in the use of virtual reality to expose patients to a scenario in which social cognition can be assessed. She says: 'People with frontotemporal dementia, for instance, may experience a myriad of changes in the way they perceive, behave and interact in different social settings. Finding a social scenario that is relevant to all patients has been a real challenge.' The technology available for delivering a virtual reality experience and for tracking eye movements is yet to be perfected. Ideally, both would be delivered via a head-mounted device (HMD), but Brotherhood notes: 'Eye tracking needs to be available in a HMD and it would certainly make testing much simpler. In addition, we could incorporate sensors to measure head movements towards or away from a stimulus, which would add even greater depth to the test data we can gather.'

INSPIRING MORE DEMENTIA RESEARCH

The C-PLACID team is hopeful that their work will improve diagnosis and treatment of individuals with dementia and inspire other scientists to work in this field. As Crutch says: 'By elevating the assessment of cognition to the same level as neuroimaging, we imagine researchers may begin to develop new measures of cognition and to study how all these aspects of cognitive performance relate to one another.' Crutch cites an example from their own work: 'We have noted that when testing overt behavioural responses, we have also been able to record some covert aspects of performance, such as cognitive effort. This can give us information on how a patient is reacting to the experimental test setting and enable adaptations and standards to be developed.'

Dr Neil Oxtoby, a research scientist from the Centre for Medical Image Computing at UCL, sees the C-PLACID computational approach being applied more widely: 'We believe that computational platforms for quantitative assessment of disease progression are the next step for modern healthcare across a whole range of diseases.' Large amounts of digital data are now available for many conditions and thus can be interrogated using machine learning and artificial intelligence platforms. He notes: 'All the big IT companies are involved in developing systems for analysing digital health records and providing data-driven patient care in hospitals. C-PLACID is part of that movement.' Brotherhood is also hopeful that their work will lead to technological advances that will facilitate the gathering of more cognitive data, such as body-mounted sensors and improved ways of synchronising different inputs.

Project Insights

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BIO

Sebastian Crutch is a neuropsychologist and professorial research associate at the Dementia Research Centre, UCL Institute of Neurology. His research focuses on rare and young-onset dementias, exploring topics such as dementia-related visual impairment, computational approaches to improving cognitive assessment, and reading and balance problems. Currently, he directs the Created Out of Mind 2016-2018 dementia and arts residency at The Hub, Wellcome Collection, which aims to shape and enrich public and professional perceptions of the dementias and explore the opportunities afforded by collaborative, interdisciplinary, publicly-situated research.

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