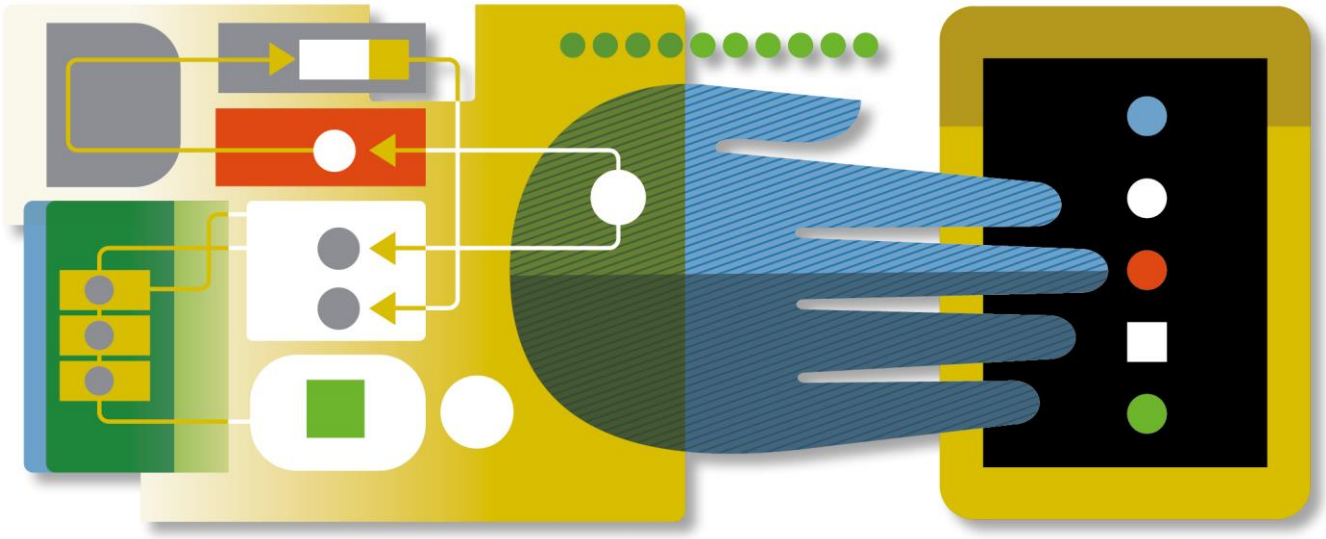
CAMBRIDGE COGNITION

Cantab Mobile

A Scientific and Clinical Review



CANTAB

Makes sense.

Contents

Cantab Mobile is an iPad-based test from Cambridge Cognition allowing clinicians to improve assessment rates of those at risk of dementia – without needing additional resources – by more accurately detecting the earliest signs of clinically-relevant memory problems and to enable more timely and informed referrals into secondary care.

Tests are simple to set up and use, typically taking around 10 minutes to complete; an audio soundtrack, available in 20 languages talks patients through each step, no reading or writing is required; and results are automatically scored and recorded with a full audit trail. In addition, test results are automatically adjusted for a patient's age, gender and education in line with NICE recommendations. To date over 10,000 NHS patients have been successfully assessed for mild cognitive impairment and Alzheimer's disease with Cantab Mobile.

For more information visit www.cantab.com/mobile

Scientific Background

Cantab Mobile is based on technology that has been used in scientific research for 25 years. Invented at the University of Cambridge, the Paired Associates Learning (PAL) test was developed as a way of assessing episodic memory without language barriers. PAL has been used worldwide in top universities and clinics, and by scientists developing new medicines for Alzheimer's and other diseases. Research using the PAL test has led to 175 publications in peer-reviewed scientific and medical journals.

Cantab Mobile uses the knowledge gained from this heritage of research to enable accurate memory assessment in primary care. Some examples of this include:

Sensitive to Alzheimer's disease and mild cognitive impairment

Problems with episodic memory can be the first warning signs of Alzheimer's disease and among patients with mild cognitive impairment (MCI), tests of episodic memory are the best predictors of subsequent conversion to Alzheimer's disease[1]. Across a number of studies, the PAL test shows a sensitivity of 100% and a specificity of 92% in differentiating mild Alzheimer's disease from healthy older adults.

Differentiating MCI is more difficult, since not all the MCI group actually have Alzheimer's or another underlying cognitive disease. Nonetheless, the OPTIMA study has reported that PAL scores have a sensitivity of 0.83 and a specificity of 0.82 in differentiating adults with MCI from healthy older adults[5].

In a recent study at the University of Tasmania, patients with amnestic MCI showed poorer performance on the PAL than either controls or non-amnestic MCI patients at baseline. When reassessed 10 months later, patients with amnestic MCI had worsened by an average of four errors at the six-pattern stage. In contrast, the PAL scores of patients with non-amnestic MCI, who are at lower risk for Alzheimer's disease, changed by less than one error[18].

Performance depends on the brain regions that are affected first in Alzheimer's disease

The PAL test depends on the integrity of the hippocampal formation, the brain structure which is affected first in Alzheimer's disease. Neuroimaging studies of healthy older adults completing the PAL test have shown that bilateral hippocampal activation increases as the number of patterns that the patient must remember goes up[11, 15].

Clinical implications of timely episodic memory assessment

Timely diagnosis of dementia-related diseases is a Department of Health priority[7]. Dementia has a huge impact on people living with the condition, their families and carers, and costs the healthcare system an estimated £19 billion a year, more than the costs of cancer, heart disease and stroke[22].

Surveys show us that people with dementia would like early diagnosis, despite this more than half of people living with dementia do not have a diagnosis. And we know that with early intervention, and access to the right services and support, people with dementia can continue to live well for many years[6]. Timely detection of dementia-related diseases can make healthcare services more sustainable, reducing the costs of avoidable hospital care, unnecessary GP consultations and the need for social care[6].

At the early stages of a dementia related disease, it can be difficult to determine if an individual has a clinically-relevant memory problem, or can be classified as a 'worried well' individual. By identifying the earliest signs of cognitive impairment in Alzheimer's disease (episodic memory loss), Cantab Mobile can help facilitate more accurate referrals to secondary care and reduce the time to make a formal diagnosis.

Identification of MCI is also consistent with NHS NICE guidelines stating that 'primary healthcare staff should consider referring people who show signs of MCI for assessment by memory assessment services to aid early identification of dementia, because more than 50% of people with MCI later develop dementia[4, 9].

NICE also recommends follow-up of people identified with MCI to monitor cognitive decline and other signs of possible dementia in order to diagnose and plan care at an early stage [9, 10]. As a sensitive test of episodic memory Cantab Mobile can support this.

Differentiates symptoms of depression from MCI and dementia with 98% accuracy

The PAL test is highly sensitive to the early signs of dementia but is generally unaffected by the symptoms of depression. Swainson et al. (2001) showed that individuals with major unipolar depression show PAL scores similar to age-matched healthy controls, with little overlap between these groups and patients with mild Alzheimer's disease[20]. In addition, Cantab Mobile includes a standardized assessment of depression, the Geriatric Depression Scale[23]. This well-validated scale allows self-reported mood symptoms to be assessed in multiple languages.

Clinical implications of symptom differentiation

With Cantab Mobile, doctors can confidently differentiate mood disorders from memory impairment. The built in Geriatric Depression Scale (GDS-15), provides a full picture of both memory performance and mood to support a more accurate and efficient assessment process to separate the symptoms of dementia from depression.

Results take into account a large normative database

Cantab Mobile is based on a dataset of more than 5,000 older adults collected through a number of different UK research projects. This large dataset allows a very accurate assessment of the expected level of memory performance for any individual aged 50 to 90 years.

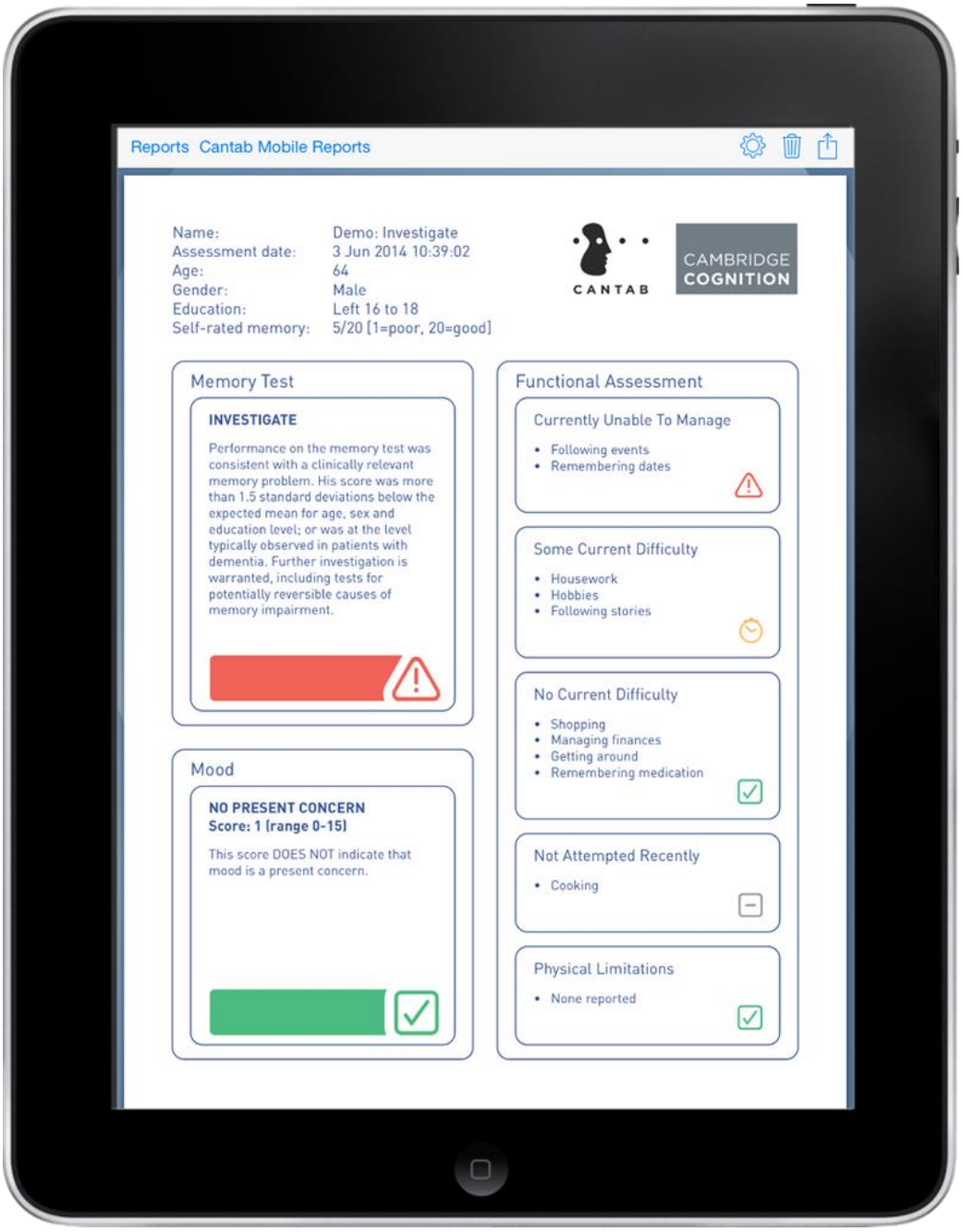
A patient's score is automatically adjusted to take into account the effects of age, education and gender on memory. Women make slightly fewer errors on the PAL test than men, and people who have spent longer in education tend to have slightly better scores. These effects are relatively small compared to the effect of ageing, shown below. Episodic memory tends to develop in early childhood and remains relatively stable through mid-life, before worsening in later life.

Clinical implications of normative database

NICE guideline for cognitive assessment in dementia state that relevant demographic factors such as age, gender, and educational level can be taken into account when deciding whether a person's score is outside their personal expected range[9]. Cantab Mobile accounts for this automatically which is strength in comparison to many brief cognitive tools[2].

Because this particular memory test is non-verbal, it is culturally neutral (i.e. previous experience, language, and culture should not affect performance) and suitable for use in non-literate or ethnic minority groups.

Example Cantab Mobile report:



A review of common cognitive assessments

There are a variety of brief cognitive assessment tools that are currently available for use in primary care settings, here we review the strengths and weaknesses of each.

6CIT

The Six Item Cognitive Impairment Test (6CIT) is a questionnaire often used to screen for dementia. The 6CIT is scored out of 28 and dementia is typically indicated by a score of 8 points or more. One study found 6CIT performed well as a screening tool in older hospital patients[21]. However, a recent large study published in *Aging and Mental Health*, reported that the 6CIT was not recommended as a dementia screening instrument in primary care, due to poor psychometric properties in a real-world setting[13].

MMSE

The Mini Mental State Examination (MMSE) has been used as a screening tool of cognitive function in clinical practice worldwide. Cut-offs of 23/24 out of 30, suggest significant cognitive impairment. However, it has low sensitivity to early dementia and MCI, and performance may be influenced by age, education, and ethnicity[19]. It has recently become copyrighted and is less widely used in primary care settings.

Cantab Mobile

The Cantab Mobile test (Paired Associates Learning - PAL) is a sensitive test of episodic memory. Episodic memory impairments are one of the earliest signs of Alzheimer's disease and other dementias. Many older adults who appear normal on the 6CIT, GPCOG and MMSE will show clinically-relevant impairments on the PAL test. This is particularly the case for the younger-old and those with high levels of education and occupational attainment. PAL is particularly sensitive to the earliest signs of cognitive impairment among individuals who do not yet have dementia, older adults with subjective memory complaints, and patients with signs of mild cognitive impairment (MCI). Therefore, Cantab Mobile is an ideal tool for diagnostic pathways that are aiming to identify patients with MCI, or detect dementia-related diseases at the earliest possible stage.

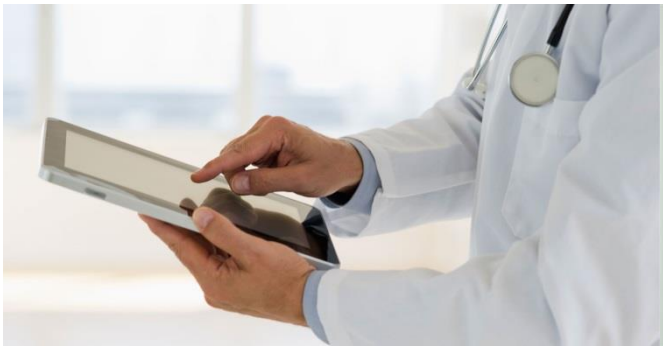
Cognitive test comparison

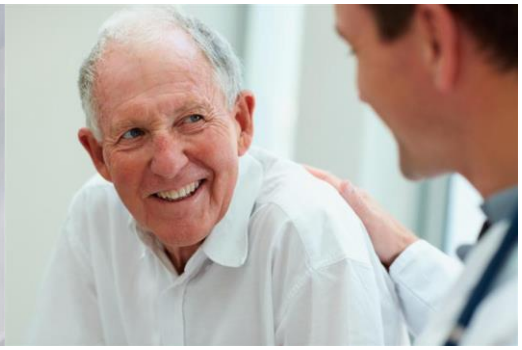
	6CIT	GPCOG	MMSE	Cantab Mobile
Test format	Paper and pencil	Paper and pencil	Paper and pencil	Touchscreen
Domains assessed	Orientation Arithmetic Verbal recall	Orientation Clock drawing Verbal recall	Orientation Registration, Attention and calculation Language Verbal recall	Visual episodic memory Depression Activities of daily living
Resource needed to complete	Trained health care professional needed to administer, score and report	Trained health care professional needed to administer, score and report	Trained health care professional needed to administer, score and report	Any staff member can administer the test. Instant reporting and scoring generated for audit trail
Sensitivity to dementia (primary care/community population)	Low to moderate 40-45% sensitivity and 92% specificity to dementia[13] Mild dementia sensitivity 78% specificity 100%[3]	Moderate to high 85% sensitivity and 86% specificity to dementia[2]	Moderate to high 88% sensitivity and 86% specificity to detect dementia[14]	**High** 100% sensitivity and 92% specificity to mild-moderate Alzheimer's dementia
Sensitivity to MCI (primary care/community population)	Not reported	Not fully established (Larner, 2013)	Low (Lonie et al., 2009)	**Moderate to high** 83% sensitivity and 82% specificity in differentiating adults with MCI from healthy adults[5]
Sensitivity to patient's age, gender and education	NICE recommends clinicians should take into account	NICE recommends clinicians should take into account	NICE recommends clinicians should take into account	Automatically adjusted for age, gender, education from 5000+ normative data
Sensitivity to signs of depression	Low	Low	Low	**High**

What information should be given to patients before they take the Cantab Mobile test?

Patients who present with a memory concern can be told that Cantab Mobile is a way for you to objectively measure their memory and that if their results show that further investigation is required you may conduct a blood test to look for reversible causes of memory difficulties, such as vitamin deficiencies or thyroid problems. At the stage where you get the results from the blood tests, if you are going to refer the patient, you can inform the patient that you are going to investigate their memory further by sending them to a memory clinic, where they will have some more tests and possibly also a brain scan. It is usually at the memory clinic level that a diagnosis of either MCI or a dementia-related disease will be made.

Cantab Mobile is sensitive to MCI, unlike traditional cognitive tests often used in primary care, such as MMSE, GPCOG, 6CIT. Therefore, you may find an increase in the number of patients you refer to the memory clinic who are subsequently diagnosed with MCI. It is at this point that you may want to give patients information about this condition – although these patients should be followed up by your memory clinic regularly, according to the NICE guidelines.





Health economics of Cantab Mobile

Two research studies presented at the Alzheimer's Association International Conference 2014 in Copenhagen highlight the potential cost savings that could be achieved by the use of Cantab Mobile in the assessment of patients who present with subjective memory complaints in the UK[8, 16].

Financial analysts estimate from these studies that the minimum cost saving to the NHS of implementing Cantab Mobile is £33 million over the next 7 years[24].

Impact of sensitivity and specificity on GP diagnostic costs

An economic model compared the two most commonly used pencil and paper tests, MMSE (88% sensitivity, 86% specificity) and GPCOG (85% sensitivity, 86% specificity) with Cantab Mobile (100% sensitivity, 92% specificity). The pencil and paper tests resulted in a saving of £158 per patient compared to no test at all; Cantab Mobile resulted in a saving of £165 per patient, or an additional £700 per 100 patients.

Impact of Cantab Mobile of total diagnostic costs

The cost effectiveness of introducing Cantab Mobile into standard diagnostic pathways in the UK for patients presenting with memory complaints was calculated with the analysis concluding that the ability of Cantab Mobile to identify patients that did not need to be referred to costly dementia services, and to treat them accordingly, reduced diagnostic costs by 40%, from £42,210 per 100 patients to £25,666.

The model estimated that 47% of people presenting to primary care with subjective memory complaints are likely to be 'worried well' and an additional 15% to have depression and not dementia. Cantab Mobile is capable of differentiating healthy patients, patients with depression and patients with mild cognitive impairment or dementia with 98% accuracy. Therefore, less than half of patients presenting to primary care with memory complaints would be appropriately referred to dementia diagnostic services using the assessment.

Economic implications

That a test which has a higher sensitivity and specificity saves money, through more accurate and earlier identification of patients with cognitive function problems to enter costly dementia services, is no surprise; however, the extent of the cost saving has now been quantified.

With an estimated additional dementia patients expected to be diagnosed by 2021 in the UK, analysts estimate the reduction in diagnostic costs if Cantab Mobile were fully adopted to be in excess of £33m.

Clinical use in the NHS

Currently, up to 1,000 Cantab Mobile assessments are being carried out each month within the NHS to raise the level of timely diagnosis and reduce inappropriate referrals.

Of the first 10,000 Cantab Mobile tests completed, 25% of patients were identified as 'red' showing clinically significant memory problems. Therefore, current data suggests that only about a quarter of patients presenting to these primary care practices with concerns about their memory require further investigation.

Feedback from primary care users indicates that Cantab Mobile assessments are often administered by nurses and support staff, freeing up doctors' time and preventing avoidable consultancies and reducing practitioner workload. The instant report and audit trail has also been highlighted as a useful, timesaving feature.

"The Dementia Challenge is huge, but there is **hope** in the extraordinary work of ***Cambridge Cognition***, working to develop new tests for Alzheimer's disease."

Prime Minister David Cameron
Speaking at the G8 Dementia Summit

"Cantab Mobile is accurate, easy to use and quick to administer. The automatic scoring provides instant reports and gives peace of mind to patients. This enhances the services we offer to our patients who have dementia, their family and carers."
Joanne Liversidge, Primary Care Liaison Nurse for Dementia

"We now have a tool that sensitively detects the earliest signs of dementia. This frees up capacity in the memory service and reduces unnecessary stress for patients and their families."
Gary McFegan, Associate - Dementia and Carers, Kent and Medway Commissioning Support Unit

"Our Dementia diagnosis rate has improved from 39% to 46.4%. Cantab Mobile has raised awareness of mild cognitive impairment in primary care and actively encourages practices to assess patients at an early stage."
Debbie Mayor, Dementia Programme Manager, Havering Clinical Commissioning Group

"The instructions are very clear, easy to follow and it is a non-threatening experience for patients. The relief is obvious when positive results are shared."
Dr Chris Mimnagh, Kirby GP & Director of Strategy & Innovation for Aintree University Hospitals NHS Foundation Trust

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Detecting dementia before the damage is done.

Makes sense.