

## Impact case study (REF3)

<b>Institution:</b> University of Edinburgh		
<b>Unit of Assessment:</b> 4		
<b>Title of case study:</b> C: A standardised cognitive screening tool to underpin personalised care for people with motor neurone disease worldwide		
<b>Period when the underpinning research was undertaken:</b> 2011 – 2020		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Sharon Abrahams Thomas Bak	Personal Chair of Neuropsychology Reader	2004 – present 2006 – present
<b>Period when the claimed impact occurred:</b> 2014 – 2020		
<b>Is this case study continued from a case study submitted in 2014?</b> N		
<b>1. Summary of the impact</b>		
<p><b>Underpinning Research:</b> Edinburgh Neuroscience-led research characterised a specific profile of cognitive and behavioural changes in patients with motor neurone disease (MND), and developed and validated a bespoke assessment tool, the Edinburgh Cognitive and Behavioural amyotrophic lateral sclerosis (ALS) Screen (ECAS).</p>		
<p><b>Significance and Reach of Impact:</b> The UK's National Institute for Health and Care Excellence (NICE) clinical guidelines for the assessment and management of MND were updated in 2016 to recommend cognitive screening for all MND patients at diagnosis, based on Edinburgh Neuroscience research. The MND Association (since 2014), Royal College of Nursing (2016) and European Network to Cure ALS (2013) recommend that all patients with MND be assessed with the ECAS.</p>		
<p>Some 600 MND healthcare professionals from 16 countries have been trained and certified to administer the ECAS. A cognitive assessment using the ECAS is now routinely carried out with all new MND diagnoses in Scotland, at 21 of 22 MND centres across the UK (June 2018 data) and at 45 MND services in 25 countries across the world. The ECAS has been standardised across 22 languages and is being used as an outcome measure in at least 13 international clinical drug trials testing effective therapies for MND.</p>		
<p>Patients benefit from cognitive assessments as this enables clinicians to tailor subsequent care to their specific needs, for example by aiding communication, alerting other relevant healthcare professionals and supporting decision-making around treatment choices.</p>		
<b>2. Underpinning Research</b>		
<b>The Challenge: Patients with MND have cognitive and behavioural impairments</b>		
<p>MND is a progressive neurological disorder where motor neurons gradually degenerate causing muscles to weaken and ultimately waste away. Several variations exist, with amyotrophic lateral sclerosis (ALS) being the most common. MND affects 5,000 adults in the UK at any one time, with a lifetime risk of 1/300.</p>		
<p>Due to its primary presentation, MND has traditionally been considered as a disease of the motor system. However, Edinburgh Neuroscience researchers have demonstrated that MND can also impact on the patients' cognition and behaviour. Using experimental neuropsychological techniques, they have identified a specific pattern of cognitive and behavioural problems, particularly in those with mild cognitive impairment without dementia. This profile is characterised by deficits in executive functions (not speed of information processing) [3.1], emotional and social cognition [3.2] and language (word finding and spelling) [3.3]. They also showed that cognitive and/or behaviour changes become more common as the disease progresses; at the early stages of the disease, 42% of patients show cognitive/behavioural changes, while at the later stages, this rises to 80%, highlighting the prominence of these problems [3.4].</p>		

Addressing a possible cause, Edinburgh Neuroscience researchers were the first to demonstrate the neural underpinnings of different types of executive dysfunction in MND. Using diffusion tensor magnetic resonance imaging, they showed that the integrity of different white matter pathways were related to problems with letter fluency and dividing attention between two objects [3.1].

### **The ECAS is a standardised screening tool for cognitive/behavioural changes in MND**

Despite these findings, the lack of a standardised tool meant that it was not possible to determine the cognitive status of patients with MND attending clinics, and consequently these changes could not be taken into account in care planning. To address this, in 2011, the Edinburgh Neuroscience team was awarded funding from the MND Association to develop a bespoke and standardised screening tool for cognitive and behavioural changes in MND.

This work resulted in the development of the ECAS, a 20-minute assessment which provides an accurate and comprehensive profile of cognitive and behavioural changes in MND by assessing multiple cognitive domains, with a focus on functions typically affected in MND. These problems may manifest as difficulties in planning and decision-making, using communication aids (due to word-finding and spelling errors), and problems understanding social interactions with family, carers and clinicians. Thus, understanding these problems can pinpoint particular care needs of the person [5.6]. Furthermore, uniquely among neuropsychological assessments for MND, the ECAS was designed to accommodate for physical disability, as cognitive impairments are not exacerbated by problems with spelling or speaking, so it can be undertaken by most patients at any stage of illness.

Importantly, the ECAS was designed to be used by a range of health professionals, who may have input into a multidisciplinary clinic, including psychologists, nurses, occupational and speech and language therapists, neurologists and palliative care specialists; it does not necessarily require a neuropsychologist to administer it.

### **Validation of the ECAS**

The Edinburgh Neuroscience researchers carried out extensive validation of the ECAS against gold standard neuropsychology assessment across the domains of fluency, executive function, language, memory and visuospatial function, and showed that it has a minimum of 85% sensitivity and 85% specificity, using published abnormality cut-off scores, in identifying not only which patients have impairment, but also the type of impairment [3.3; 3.5]. Of patients with no overt signs of dementia, 33% showed cognitive impairment in domains of fluency and executive and/or language functions, the latter being the most prominent [3.5].

The researchers further validated the pattern of deficits and sensitivity of the ECAS to detect brain pathology by analysing post-mortem brains of 27 MND patients without dementia, who had been assessed with the ECAS during life. MND-specific pathology was found in the frontal and temporal parts of the brain, outside of the motor system, in all patients who had exhibited cognitive impairment on the ECAS (positive predictive value of 100%; sensitivity of 44%). The ECAS domain scores (executive functions, language and fluency) also predicted pathology with 100% specificity in distinct brain regions associated with these functions [3.6].

### **3. References to the research**

[3.1] LD Pettit, ME Bastin, C Smith, TH Bak, TH Gillingwater, S Abrahams, 2013. Executive deficits, not processing speed relates to abnormalities in distinct prefrontal tracts in amyotrophic lateral sclerosis. *Brain* 136(11), 3290-3304 [doi: 10.1093/brain/awt243](https://doi.org/10.1093/brain/awt243)

[3.2] Girardi, A., MacPherson, S. E., & Abrahams, S. (2011). Deficits in emotional and social cognition in amyotrophic lateral sclerosis. *Neuropsychology*, 25(1), 53. [doi: 10.1037/a0020357](https://doi.org/10.1037/a0020357)

[3.3] Abrahams, S., Newton, J., Niven, E., Foley, J., & Bak, T. H. (2014). Screening for cognition and behaviour changes in ALS. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 15(1-2), 9-14. [doi: 10.3109/21678421.2013.805784](https://doi.org/10.3109/21678421.2013.805784)

[3.4] Crockford, C., Newton, J., Lonergan, K., Chiwera, T., Booth, T., Chandran, S., Colville, S., Heverin, M., Mays, I., Pal, S., Pender, N., Pinto-Grau, M., Radakovic, R., Shaw, C. E., Stephenson, L., Swingler, R. J., Vajda, A., Al-Chalabi, A., Hardiman, O., & Abrahams, S. (2018). ALS Specific cognitive and behaviour changes associated with advancing disease stage in ALS. *Neurology*, 91(15), [e1370]. [doi: 10.1212/WNL.00000000000006317](https://doi.org/10.1212/WNL.00000000000006317)

[3.5] Niven, E., Newton, J., Foley, J., Colville, S., Swingler, R., Chandran, S., Bak, T.H. & Abrahams, S. (2015). Validation of the Edinburgh Cognitive and Behavioural Amyotrophic Lateral Sclerosis Screen (ECAS): a cognitive tool for motor disorders. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 16(3-4), 172-179. [doi: 10.3109/21678421.2015.1030430](https://doi.org/10.3109/21678421.2015.1030430)

[3.6] Gregory, J., McDade, K., Bak, T., Pal, S., Chandran, S., Smith, C., & Abrahams, S. (2019). Executive, language and fluency dysfunction are markers of localised TDP-43 cerebral pathology in non-demented ALS. *Journal of Neurology, Neurosurgery & Psychiatry*, 1-9. [doi: 10.1136/jnnp-2019-320807](https://doi.org/10.1136/jnnp-2019-320807)

#### 4. Details of the impact

##### Impact on guidelines

In 2016, NICE updated its guidelines for assessment and management of MND [5.1a]. Abrahams was a co-opted expert advisor on the Guideline Development Group (GDG), and the only psychologist on the group [5.1b]. The Chair of the GDG described the reasons for asking her to join the GDG: “*Professor Abrahams’ [...] research at Edinburgh was most pertinent to the GDG’s discussion on this topic.*” [5.1c].

As a result of the consensus reached by the GDG, the published NICE guidelines recommended, for the first time, that all individuals with MND should be offered a cognitive assessment at diagnosis by a member of the multidisciplinary care team and that all subsequent care should be tailored to their identified cognitive impairments [5.1a]. The Chair stated: “*The knowledge that a standardised tool existed to explore these changes gave the GDG additional confidence that this recommendation could be executed in practice.*” [5.1c].

The UK’s largest MND charity, MND Association (MNDA), an important source of information for people with MND, carers and families and clinicians, also recommends cognitive assessments for all patients with MND using the ECAS. They publish comprehensive information booklets for 3 audiences: patients and carers (2015, updated in 2020) [5.2a], healthcare professionals in secondary care (2014) [5.2b] and GP primary care teams (2015) [5.2c]. All specifically recommend the ECAS for diagnosing cognitive and behavioural changes, and the healthcare professionals’ booklet includes a detailed 2-page description of the ECAS and its use, citing 11 Edinburgh publications. Since MNDA began collecting data in January 2017, the patient and carer guide has been downloaded 3,250 times (2,028 hard copy orders), the secondary care guide 3,369 times (1,837 orders) and the primary care guide 3,449 times (3,960 orders) [August 2020 data; 5.2d]. The Royal College of Nursing also includes a page on cognitive changes in their list of resources for nurses and other healthcare professionals (published in 2016) and explicitly recommends using the ECAS to screen for signs of cognitive or behavioural change in patients with MND [5.3].

##### Impact on professional training

In 2016, MNDA commissioned the Edinburgh Neuroscience team to develop a national training programme to enable cognitive screening of all patients with MND in the UK, in accordance with the NICE guidelines. This led to the development of a day-long Masterclass on how to administer the ECAS and interpret its results. The masterclass was delivered to 353 MND healthcare professionals in England, Wales and Northern Ireland [5.4] and a further 16

in Scotland, reaching all 22 MND-recognised care centres/networks in England, Wales, and Northern Ireland and 11 MND clinics in Scotland. 85 of the participants were clinical nurse specialists who provide front-line NHS clinical support throughout the disease and help coordinate care; the rest were occupational therapists (39%), speech and language therapists (18%), physiotherapists (5%), psychologists (5%) and dieticians (2%). Importantly, this programme not only trained and certified key MND healthcare professionals to administer the ECAS, but also actively facilitated links with their local clinical neuropsychology services [5.4].

### **Impact on clinical practice**

Accounting for MND patients' cognitive needs is now the standard of care in the UK. In Scotland, this is managed through a "dual care pathway" whereby every newly diagnosed patient with MND is assessed using the ECAS either by their local NHS neuropsychology services, or a member of the MND multidisciplinary care team supervised by their local neuropsychologist [5.5a]. The British Psychological Society cites this as an exemplary system of managing MND patients' cognitive needs [5.5b].

In a 2018 survey of all 22 MND care centres in the UK, 21 centres (95%) reported screening patients for cognitive and behavioural changes using the ECAS. 10 centres (45%) reported offering the ECAS to every new patient with MND [5.6].

### **Impact on health & welfare**

Use of the ECAS facilitates personalised care and leads to improved quality of life for patients with MND through enabling the multidisciplinary care team to tailor interventions and support to the particular needs of each patient and their carers. This was illustrated by a qualitative study consisting of semi-structured interviews with 20 consultant neurologists, clinical neuropsychologists, patients and carers across the UK [5.6]. This study indicated that use of the ECAS 1) raises awareness about cognitive/behavioural changes among patients, carers and healthcare professionals, 2) validates and reassures the patients' and carers' experience by providing an objective measure of any changes 3) aids understanding of the patients' presentation by identifying changes that may be underestimated by the healthcare team and 4) ultimately informs clinical decision-making. The latter includes decisions over suitability and type of interventions, prompting early discussions of end-of-life care, improving care by informing other healthcare professionals to adjust support to the needs of the patient, and identifying carers' support needs [5.6]. A consultant neurologist interviewed for the study gave an example:

*"You're [...] being more proactive in terms of getting patients' opinions of what they want done if there's evidence of cognitive impairment...if people are likely to have significant behavioural disturbance and are not going to be able to [...] understand what a gastrostomy is or take part in it."* [5.6]

### **International uptake of the ECAS**

The ECAS has been implemented into routine clinical practice across Europe, driven by the European Network for the Cure of ALS (ENCALS), an EU-funded group of 64 leading MND centres in 19 countries. ENCAL's adoption of the ECAS as the recommended assessment tool in July 2013 led to its widespread subsequent implementation in ENCAL-affiliated centres; the Chair and Deputy Chair confirmed in 2020: *"ECAS is now recognized as the gold standard of cognitive assessment in ALS, as it is more sensitive and specific than any other available screening tool for ALS. The information it provides is used to support patients, determine and adapt treatments and provide specialised care for people with ALS according to their cognitive difficulties."* [5.7]

This widespread implementation of the ECAS in ENCAL centres has been enabled by the availability of the ECAS in 22 different languages. These are freely available on a dedicated ECAS website [5.8a], which was launched in January 2018 and has received more than 41,500 visits from 124 countries between then and December 2020 [5.8b].

International uptake of the ECAS has been further facilitated by an online, ENCALs-certified, training programme aimed at healthcare professionals wishing to start using the ECAS in their practice. By July 2020, this had certified 230 healthcare professionals from 16 countries across Europe, Australia, USA and Canada to use the ECAS in clinical settings [5.8b].

In 2019, an international survey of MND centres around the world asked about the proportion of new and existing ALS patients that undergo a cognitive assessment, what the results are used for, and how they inform patient care. 80 responses were received from the major MND clinical centres in 25 countries outside the UK (including ENCALs centres). 45 (56%) centres reported using the ECAS in routine clinical practice. Combined, these 45 centres treat 7,434 patients per year and receive 3,218 new patients per year. Importantly, 43 (96%) of these centres reported that ECAS results directly inform their clinical practice, and 72% agreed or strongly agreed that MND patients screened for cognitive changes receive better clinical care [5.9].

### **The ECAS is the standard outcome measure in international clinical trials for MND**

The ECAS is one of the core recommended tools in the US National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements guidelines for clinical trials [5.10a] and has thus far been used in 8 drug trials for MND [5.10b]. The largest of these, an ongoing Phase III clinical trial of arimocloamol, has so far randomised 245 ALS patients across 11 countries, involving 9 translations of the ECAS and training 72 ECAS interviewers. The ECAS is also an outcome measure in the innovative Edinburgh-led UK-wide multi-arm adaptive trial MND-SMART [5.10b].

In Europe, the ECAS is the agreed outcome measure for cognitive/behavioural changes in the protocol for TRICALS [5.10c], the largest European research initiative to find a cure for ALS, involving 42 research centres in 16 countries. TRICALS is currently running an additional 5 clinical trials to identify effective treatments for MND [5.10d].

### **5. Sources to corroborate the impact**

- [5.1] a. NICE guideline CG42 Motor Neurone Disease: assessment and management (recommendation 1.3 on p. 9) b. GDG list of members c. Letter of support from Chair of Guideline Development Group
- [5.2] MNDA guidelines for identification and management of cognitive changes: a. For patients b. For healthcare professionals in secondary care c. For GPs and primary care teams d. Download data of all 3 guides
- [5.3] Royal College of Nursing resource on MND: cognitive changes page
- [5.4] End-of-grant report to MNDA describing training activities
- [5.5] a. Letter from Scotland's National Lead MND Nurse b. British Psychological Society "Resources" page, describing MND pathways
- [5.6] Hodgins, F, Mulhern, S & Abrahams, S 2019. The clinical impact of the Edinburgh Cognitive and Behavioural ALS Screen (ECAS) and neuropsychological intervention in routine ALS care. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*. doi: [10.1080/21678421.2019.1674874](https://doi.org/10.1080/21678421.2019.1674874)
- [5.7] Letter of support from ENCALs Chair and Deputy Chair
- [5.8] a. [ECAS website with translations](#) b. ECAS website traffic and data from online ECAS training
- [5.9] Results of international survey of ECAS usage as poster accepted for international ALS/MND symposium (9<sup>th</sup>-11<sup>th</sup> December 2020)
- [5.10] Adoption of ECAS into clinical drug trial protocols: a. NINDS Common Data Elements b. 8 trials using ECAS: Arimocloamol in ALS (NCT03491462); EMERALD (NCT03690791), ROCK-ALS (NCT03792490), FAIR-ALS (NCT03293069); CU(II)ATSM for MND (NCT04082832); MIROCALS (NCT03039673); IC14 for Treatment of Amyotrophic Lateral Sclerosis (NCT03508453); MND-SMART (NCT04302870) c. ECAS as the agreed outcome measure for TRICALS clinical trials d. [TRICALS website showing 5 additional trials](#)