

Cognition services in MS: Where next?

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Objective

ACNR brought together an expert panel to review the current issues relating to the management of cognitive function in people living with multiple sclerosis, and the impact this has on their quality of life.

Introduction

DAWN LANGDON

Multiple sclerosis (MS) is an autoimmune-mediated neurodegenerative disease of the central nervous system associated with a range of physical and mental symptoms [1]. Cognition is one of the “invisible symptoms” of MS [2]. Although it clearly has a significant impact on the lives of people with MS, it is not well understood or quantified in clinical practice [3].

In people with MS, the aspects of cognition most likely to be affected are memory, information processing speed, and problem solving. Problems in these areas may not be apparent to friends and family, or even to healthcare professionals. Yet many aspects of life are adversely affected by cognitive dysfunction, including employment, relationships, daily activities, physical independence and disease management. In fact, we know that employment is greatly affected for people with MS, even at very low levels of physical disability [4], and cognition is a significant part of this. There are also key safety issues related to cognition, such as driving ability or the risk of falls.

Importantly, cognition can also influence a person’s disease management, leading to complications in medical decisions, rehabilitation benefit, and their coping skills [5]. The range of therapies available for MS have complex benefit-risk profiles, and engagement in informed consent and credible shared decision making is difficult for people with cognitive impairment. People who understand their medications are more likely to comply with their treatment schedule [6]. Cognition is not closely related to other disease variables, including MRI and so traditional medical investigations are not good indicators of an individual’s cognitive status [7]. Self-reported cognition is a helpful way to understand patients’ experience, but this is confounded by a number of psychosocial factors such as mood [8]. In order to fully understand cognition and measure the impact of therapy, a more objective measure is needed. For example, BICAMS (the Brief International Cognitive Assessment for Multiple Sclerosis) is a tool that can be administered in 15 minutes by most health professionals, and requires no specialist training [9].

There are a range of options for management of MS cognitive problems. Information for patients is

Expert Panel

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 Noreen Barker, MS Nurse
 Nathalie Fricker, person with MS
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a keystone [10]. Part of this is to support patients’ understanding that positive lifestyle choices can slow the progress of the disease, including cognitive impairments, the “Brain Health” agenda [11]. Besides information and support, MS clinics can protect cognition by ensuring optimal MS treatment more broadly, including early intervention [12], disease modifying therapies [13] and management of co-morbidities [14]. Cognitive rehabilitation is a promising approach to treat cognitive dysfunction in MS, gaining empirical support over the last 10 years [15]. For example, cognitive rehabilitation can induce improvements in memory function and quality of life [16]. People with MS can participate successfully in self-directed, cognitive retraining on computer, which is less expensive to provide [17].

There is widespread support for the inclusion of cognitive assessment and management in routine clinical practice, but there are significant challenges [18]. An essential factor for implementation of the pathway is allocation of time during clinic appointments and within staff workloads [19]. Unfortunately, in the short term this model is not a viable framework for the NHS, and there remains a need for a more workable solution for people with MS. The recent COVID pandemic has interrupted clinical and research activity relating to MS cognition, however restoration of services and investigations is underway [20].

This panel was set up to review the current issues relating to the management of cognitive function in people living with MS, and the impact this has on their quality of life. The group met in March 2021 to share information about

clinical challenges, and ideas for overcoming barriers.

Clinical challenges – what does the neurologist need in the clinic?

KHALED ABDEL-AZIZ

In current practice, cognitive testing is done at the individual neurologist’s discretion. A more efficient approach to detect cognitive symptoms in people with MS would be to standardise routine cognitive assessments for all patients. But there are challenges to delivering cognitive assessments, both in specialist MS clinics and general neurology services. When considering what is needed to enable cognitive assessments to be included in standard care, it is important to recognise that MS clinics already cover a vast range of items, and there are time pressures. Consultant neurology follow-up appointments are typically 10-20 minutes, and cover relapses and symptom changes, scans, compliance, safety and side effects, as well as a physical examination and discussion of any new management options. However, there is value in including cognition as standard. Cognitive impairment is reported in 40-70% of people with MS and there is evidence that early cognitive impairment can predict clinical course [21,22]. Screening assists timely detection of cognitive deficits, thereby allowing patients to be referred for support at an earlier stage.

The current recommendation is that cognitive symptoms in MS should be screened annually [23,24], but this is difficult in practice. Gold-standard assessments such as MACFIMS (Minimal Assessment of Cognitive Function in MS) are time-consuming – taking up to 90 minutes with a neuropsychologist; measures such as Rao’s take 30 minutes to administer, but at the expense of sensitivity. For an average clinic (~10 patients), this would require an additional capacity of 5-15 hours. There is an additional need to look alongside for confounding secondary factors such as depression or sleep problems. More practical options use shorter screening tools that can be delivered by any member of the healthcare team: BICAMS takes only 15 minutes, with comparable sensitivity to MACFIMS, or the SDMT (Symbol Digit Modalities Test) only five minutes. A quiet environment is also needed for cognitive screening to minimise distractions during timed assessments, but the reality of an NHS clinic is that it can be noisy, and there are constant interruptions. Patients may also bring partners or children with them.

Computer-based, self-administered tests may solve time issues [25,26,27], but a consensus is needed on how these can be used. Potential

advantages in addition to time savings in clinic include reduced inter-rater variability; drawbacks are uncontrolled test environments, and exclusion of patients without tablets or smart phones. In the future, perhaps hospital-based test centres run by a small number of staff could assess patients en masse. This would create a controlled environment, and could be combined with self-administered screening for depression, anxiety and fatigue. Although this would require initial investment, there would be long-term cost-savings in clinic and staff time.

Practical issues and daily management – what does the MS nurse see?

NOREEN BARKER

The role of the MS Specialist Nurse in the care of people with MS has changed over the past two decades, with the evolution and wider availability of disease-modifying therapies (DMT). MS Specialist Nurses see a range of severities of cognitive impairment, which may be more silent or under reported in relapsing remitting MS compared to progressive MS, and is very unlikely to be the presenting symptom.

Cognitive impairment can be affected by comorbidities, and has a significant impact on quality of life and independence. People often mention difficulties with verbal fluency, executive functions, multi-tasking, problems with focus or concentration, and reduced processing skills. MS Specialist Nurses need to be mindful of the factors that may mimic cognitive impairment, such as acute relapse, the side effects of DMT such as progressive multifocal leukoencephalopathy, fatigue, and low mood or anxiety. Unrelated causes such as menopause or medications such as antimuscarinics can also have similar symptoms.

Education is key to improving treatment concordance and adherence, but people with cognitive impairment may struggle to process and retain information, to understand the risk-benefit of their medication, or to remember doses and follow-up appointments. Concordance with treatment can be an issue, and MS Specialist Nurses play an important role in advocating where specific treatments may be more suit-

able for them. MS Specialist nurses build good therapeutic relationships with people with MS, but this may be more challenging in larger centres with larger teams and bigger caseloads, compared to a lone MS Specialist Nurse with a smaller caseload.

MS Specialist Nurses assess and evaluate patients periodically, and where appropriate can make timely onward referrals. In partnership with the multidisciplinary team (MDT), they play a role in discussing cognition early on, to educate people with MS to recognise symptoms and legitimise cognitive concerns.

For MS Specialist Nurses, knowledge about cognitive impairment is not perceived as an issue. However, challenges exist in terms of the fear of upsetting patients and their families in bringing up cognitive problems, caseload size and mix, and the burden of DMT monitoring. Virtual consultations are becoming more common for many centres, but these appointments are not suitable for all, and there will need to be a balance of face-to-face and virtual appointments.

Overcoming barriers in relation to cognitive impairment

SUSAN HOURIHAN

Occupational therapy (OT) focuses on a person, their environment and occupation, and their participation in daily life. The aim is to either restore or compensate for lost function. Occupation as a term refers to practical and purposeful activities that allow people to live independently and have a sense of identity. These can be essential everyday tasks such as self-care, work, and leisure, all of which can be affected by cognition. Work is often the place where cognitive impairment first becomes evident. OT aims to help people maintain or modify their work, or to return to work after a relapse.

In OT, formal assessment approaches are often top-down – looking first at the occupation itself, then understanding tasks and purposeful activity, and finally the component activities. This allows a break-down of where cognitive impairment may be having an impact. Functional assessments can include the Multiple

Errands Test (MET), which evaluates the effect of executive function deficits on everyday functioning. Assessment of Motor and Processing Skills (AMPS) and Perceive, Recall, Plan, Perform (PRPP) can also be useful tools. A prompt and cue hierarchy can be useful to support learning modified tasks.

If a person with MS is referred to OT with a cognitive impairment already identified, they may come with a complete neuropsychology assessment. This is ideal as it allows the occupational therapist to commence with treatment, utilising cognitive strengths to compensate for weaknesses. However, frequently, people with MS will be referred to OT for treatment, such as fatigue management. In this case, they will often not have been assessed for cognitive function, despite cognitive impairment being present. There is a need to understand the stage each person is at in order to have a clear aim for optimal intervention. Ideally, OT should be performed as part of an MDT, including family and carers, with agreed goals and treatment planning.

Referral challenges from primary care and ongoing cognitive management

NASSIF MANSOUR

Currently, management and support for cognitive impairment in MS is lacking. The main symptoms of cognitive impairment in MS are short-term memory and attention deficit, problems with abstract conceptualisation, and slowed information processing. Many patients assume these symptoms are age- or fatigue-related, and do not report them to their GP – and often GPs themselves also make these assumptions and brush cognitive symptoms aside. This makes it difficult for patients with MS to get the support they need, and can be a driver of anxiety and fear around their disease and about their lives.

The lack of a diagnostic tool that could be used in primary care to flag patients with or at risk of cognitive impairment is another challenge. Even where cognitive impairment is suspected, support remains a problem. Referral to a Neuropsychologist takes 6-9 months and local Improving Access to Psychological

Perspectives from a person with MS – the lived experience

NATHALIE FRICKER

The patient voice is important in MS, and can help healthcare professionals to understand the daily experience of people with MS. From a patient perspective, physical versus cognitive symptoms are very different. There is traditionally an emphasis on preserving physical function and independence, with the mental impact a secondary consideration. Over time, cognition often declines, with difficulty finding the right words, and forgetfulness. Memory loss can mean people live more in the present – blurring a person's history and recall.

Some lifestyle changes that people with MS may make to protect themselves physically – such as stopping working or limiting activities – can perhaps accelerate the cognitive decline, as the brain is not kept active. Mental stimulation and exercise can help to combat mental decline. For example, reading

and discussion in a book club can help retain vocabulary. Despite the best intentions, people naturally have bad habits and lack of discipline when trying to make lifestyle changes – and those with MS can be derailed by fatigue.

Patient experience of cognition can be variable, and is difficult to predict. The brain fog is described as a feeling of knowing you cannot find the word, which can be embarrassing and awkward. Cognitive issues are easier to hide than physical issues, and many patients do not want to admit to diminishing brain power. Although generally the world is more open-minded about disabilities and impairments, there may still be a stigma attached to cognitive impairment. However, cognitive assessments are rare in clinical practice and I personally would like to see assessments done as part of the annual review.

Therapies (IAPT) services are not specialised enough to give the necessary support required.

An important role in primary care is to help the patient acknowledge an impairment, and to understand what reasonable adjustments may be required in their life. An MDT clinic in collaboration with an MS Nurse Specialist can improve identification, support and patient satisfaction. In the future, primary-care GPs need to find ways to help patients report symptoms early, and to improve awareness and diagnosis. Early support from primary care will enable patients to access specialist services, and to live well with their MS.

Research gaps – what questions do we need to answer?

CAROLYN YOUNG

The key research gaps in the field of cognitive therapies for people with MS are the development of improved treatments which generalise to affect day-to-day cognitive function, treatment selection and individualisation for patients, and achieving consensus on the definition of 'brain fog'. In addition, better understanding is needed regarding whether different patterns of treatment are needed for relapsing and progressive subtypes, and the impact of depression and anxiety.

'Brain fog' is a term used in many chronic conditions, including cancer, coeliac disease, and chronic fatigue syndrome. Among people with MS the term 'brain fog' is used to describe myriad difficulties with memory, concentration, processing capacity or speed, and motivation. Progress requires a consensus definition of MS brain fog. In some fields, brain fog is defined as an impact on processing speed, and working, visual and verbal memory. Animal studies relating to the brain fog experienced by chemotherapy patients have identified oxidative stress and apoptosis, which inhibit neuronal proliferation and differentiation, activate microglia, and affect chromatin remodelling. This leads to the aberrant expression of neurotrophic proteins in the brain (for review see Chemo brain: From discerning mechanisms to lifting the brain fog – An aging connection [28]). Changes have been shown in gene expression profiles, leading to the hypothesis that brain fog in chemotherapy has an epigenetic mechanism.[28,29] This raises an interesting question in MS, since many DMTs came from the world of oncology – are some cognitive effects driven by treatment, rather than the underlying disease? It will be important to answer this for future MS care.

In real-life clinical practice, clinicians want to know which form of cognitive rehabilitation is most likely to benefit an individual patient – or for service design, most patients in their practice – for a reasonable period of time. Interventions currently under investigation include music therapy, compensatory strategies, computer-based training

programmes and apps. However, many studies do not use intention-to-treat analyses, and the entry criteria and study duration may not be reflective of real-world patients, or unhelpful for resource planning. In designing a cognitive rehabilitation trial, it should be clear which deficit is being treated, how it can be measured, and why it is relevant to patients, society, and payers. Trials should also record the educational level of the cohort, and state whether any of the interventions affect day-to-day functioning. More research is needed to understand how routine cognitive testing can be delivered to best benefit patients, as patients may be unwilling to undergo cognitive monitoring if there is no intervention for any deficits that may be uncovered.

Unmet needs identified via the MS Trust helpline

CLAIRE WINCHESTER

People with MS often speak about the impact of cognition problems, rather than the cognitive issues themselves. The greatest impacts of cognitive problems are on relationships, employment, and study, and can be life-altering when they are a factor in family breakdown or loss of earnings.

There are several barriers to coping with cognitive problems. Traditionally, clinical focus has been on physical problems, such as those impacting walking or dexterity. Cognitive impairment is not always regularly assessed, due to the limited time and capacity in MS services. For people with MS, the terminology around cognitive problems can be scary or difficult to accept. They may not be aware of treatments or interventions that might help them live well with cognitive problems.

People with MS particularly mention difficulties with concentration, memory and organisation, which can lead to problems absorbing and acting on information. This raises issues for health literacy, and for choosing and adhering to treatment. Cognitive problems therefore have a knock-on impact on the ability of a person to self-manage their MS effectively, and can lead to worse health outcomes.

Overall, there is not enough awareness that cognitive impairment can be part of MS, and the burden falls on the patient and their family to cope with changes and mitigate the symptoms. There is also a need to consider carers and families when assessing impact, as the cognitive decline of a loved one can be challenging to cope with. People affected by cognitive problems in MS need to know what interventions might be available, and to be supported to take positive action.

Discussion

Cognitive difficulties in MS are a significant issue, and may be experienced by 65% of people living with MS [18], but the topic can

be hard to raise with health professionals. Talking about physical issues is easy for many people, but some with MS may feel they will lose a sense of themselves if they have cognitive symptoms, and this can prevent people from asking for help. Other people find it very useful to know that their symptoms are due to MS, and understanding the impact can be important in relationships and for family dynamics. Individual attitudes vary, and understanding this will guide communication and awareness in considering interventions for cognition, but demystifying cognition in MS will support many people in coming forward.

Of course, the NICE guidelines say cognition should be discussed early in the disease course, and on a regular basis [23], but in practice this does not always happen, or may be difficult to achieve. Virtual consultations have become the norm for many chronic diseases over the course of the COVID-19 pandemic, and may help to open up screening for cognition in MS – but the technology is not suitable for all. Remote delivery may be difficult for confused patients, and access may also be an issue. Where assessments are done in person, care should be taken to ensure they are delivered in optimal environments, such as asking a person to complete a single task in a quiet room [30].

Despite cognitive dysfunction being a common and disabling feature, the pathological brain changes are not fully understood [31], and precise characterisation of cognitive phenotypes is missing. Cognitive impairment is typically defined as poor performance on two or three diverse tasks, which leads to heterogeneous and ill-defined groups of people with deficits in speed, memory, or other areas [30]. However, recent research suggests defining homogeneous and clinically meaningful phenotypes may overcome some traditional limitations [32].

DeMeo and colleagues have recently identified five cognitive phenotypes that may offer utility. These are preserved cognition, mild–verbal memory/semantic fluency, mild–multidomain, severe–executive/attention, and severe–multidomain [32]. Further work recently published also suggests there is a chronological sequence in which cognitive domains become impaired, with processing speed the first area affected [33]. Clinical understanding of phenotypes and sequencing may represent an important step toward personalised treatment or rehabilitation – as well as supporting understanding of the mechanism of MS-related cognitive changes [32].

Our discussions highlight several barriers to managing cognition, particularly around identification and measurement. There is agreement that measurement is important – and MS batteries are brief by neuropsychological standards – but one-on-one testing for every patient may not be practical [30]. Some people may also resist the idea of psychometric testing when it may not be possible to correct any problems that are identified, and this testing may also not make clinical sense when

that time and resource can be used in other more impactful areas. In addition, we must be careful to develop scores and assessments that can take into account a person's prior cognitive level, and an individual's cognitive needs in their daily life. It can be easy to overlook a deficit that produces a small score in a tool, but which may in fact impact the person in a very real way, for example, in their job if processing speed and memory are key elements of a role.

To improve and standardise care, there is a need to encourage a focus on cognition, and to ask about cognitive issues in people with MS. The cognition-aware healthcare professional should note discrepantly low performance and assess cognition. People with MS can be supported by presenting information in helpful ways, and monitoring disease management. Special attention should be paid to symptom management, medication adherence, and risks for falls, driving, and employment. Where needed, we should refer people to a specialist for assessment and management.

Every person – with or without MS – has

a physical and cognitive reserve. The physical reserve may depend on age or fitness, but the cognitive reserve is the amount of capacity a person has to withstand insults such as relapse or atrophy, or psychological aspects such as anxiety – and still be able to function. It is possible to build up these reserves with exercise, and work is a critical factor in maintaining cognitive reserves and self-esteem.

This could be an important factor in shaping the advice given to people with MS, since at present much is aimed towards paring back work in an effort to reduce fatigue, but this could be an iatrogenic factor in cognitive decline. There is clearly still much to consider. Improved understanding of cognitive deficits will inform research into cognitive rehabilitation, which seeks to restore cognitive functioning or teach compensatory strategies to minimise the impact on quality of life [30]. To support this, a workable clinical code and more suitable tools are needed to standardise care, and developing these should be a priority. Above all, cognition should be cherished.

Areas for potential work:

- Patient and lay carer education on cognition
- Resources for healthcare professionals
- Developing an assessment that could be delivered via an app or other technology
- Developing self-management programmes for maintaining cognitive reserve
- Position statement on managing health anxiety
- Rehabilitation programmes, including optimal dosing
- Implementation and management
- Further research

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