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Cognition in Multiple Sclerosis

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Declaration of Independence
This book is as balanced and practical as we can make it.
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List of abbreviations

BICAMS: Brief International Cognitive Assessment for Multiple Sclerosis

BRB-N: Brief Repeatable Battery of Neuropsychological Tests

BRIMMS: Benefit and Risk Information for Medication in Multiple Sclerosis

BVMT-R: Brief Visuospatial Memory Test-Revised

CAP: cognition agenda for people with multiple sclerosis

CCAMS: clinic cognition audit for multiple sclerosis

CIS: clinically isolated syndrome

CNS: central nervous system

CR: cognitive reserve

CVLT-II: California Verbal Learning Test Second Edition

DMT: disease-modifying treatment

EDSS: Expanded Disability Status Scale

HCP: healthcare professional

HR: hazard ratio

IPS: information processing speed

MACFIMS: Minimal Assessment of Cognitive Function in MS

MRI: magnetic resonance imaging

MS: multiple sclerosis

MSNQ: Multiple Sclerosis Neuropsychology Questionnaire

NHS: National Health Service

PML: progressive multifocal leukoencephalopathy

POMS: pediatric-onset multiple sclerosis

PwMS: people/person with multiple sclerosis

QoL: quality of life

RIS: radiologically isolated syndrome

RRMS: relapsing remitting multiple sclerosis

SDMT: Symbol Digit Modalities Test

SPMS: secondary progressive multiple sclerosis

Foreword

Keep this clinic handbook close by, because you will want to come back to it often. Starting with testimonies from people with cognitive impairment affected by multiple sclerosis (MS) and ending in a list of useful agencies, it covers a huge breadth.

I learnt that cognitive impairment in MS is associated with poor adherence to disease-modifying drugs and that one-fifth of drivers with MS fail driving assessments on the road. I did not know that one-third of children with MS have cognitive dysfunction, or that self-reporting of impaired thinking by patients is so inaccurate. I am persuaded that we should adopt formal neuropsychological assessments in our clinic and that the Brief International Cognitive Assessment for MS (BICAMS) is the best on offer; that it can be administered by allied health professionals makes it feasible in busy centers. And I found tips from the 'Difficult Conversations' chapter very helpful.

Carolyn Young and Dawn Langdon have been studying and writing on cognition in MS for over 20 years, as neurologist and clinical psychologist, respectively. They have distilled this experience into pithy informative chapters, which focus on how to help the person affected by MS. Whether new to the field or a veteran, this handbook has much to offer. Keep it close by.

Alasdair Coles
Professor of Neuroimmunology
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Introduction

Difficulties with cognition are an assault on ourselves and our identities. In the context of the unpredictable and often progressive course of multiple sclerosis (MS), reductions in information processing, memory function, and other mental faculties can be a heavy burden for people with MS (PwMS).[1]

We have written *Fast Facts: Cognition in Multiple Sclerosis* to support healthcare professionals (HCPs) working in MS clinics and other services. Stakeholders have told us of a need for more information for HCPs and PwMS, better assessment tools, and practical solutions and treatments.[1] In our experience, information about cognition in MS seems to lurk either in journals that are hard to reach, with the clinical implications tucked away at the end of pages of psychometric tables and graphs, or in a few weighty tomes that, although worthy, sadly not everyone has time to read and digest. With this in mind, we have curated content from the current evidence base and clinical experience for this clinic handbook, taking a pragmatic approach. Each chapter is designed to be read as a standalone text, to enhance information access for busy HCPs and facilitate integration with specific pieces of clinical work.

We begin with some quotes from PwMS and their caregiver partners, to keep the patient voice front and center. We then provide two background chapters; the first briefly outlines the cognitive domains most likely to be affected by MS and their impacts on the lives of PwMS, and the second considers the extent to which disease and other individual characteristics are related to cognitive status, and whether they can be used clinically to indicate cognitive competence. Assessment options are then outlined in Chapter 4.

The next three chapters are most likely to be frequently used to assist daily clinic work and could be used for multidisciplinary team meetings, supervision, and mentoring sessions. Chapter 5 (MS clinic management of cognition I: healthcare professional information and action) includes useful information for MS clinic staff and actions they can take to safeguard PwMS' cognition. In Chapter 6 (MS clinic management of cognition II: people with MS' engagement, information, and action), we outline communication and content strategies for more effective engagement with PwMS to mitigate the adverse effects of their cognitive difficulties on their interactions with clinic staff. We have collated some information sources designed for PwMS and indicate some self-management strategies that PwMS can adopt, along with how clinic staff can support them with these. Chapter 7 (Additional specialist input) summarizes external expert resources that might be available to you. Finally, Chapter 8 covers difficult conversations, with suggestions for how you might structure, present, and resolve sensitive matters at consultation.

We hope that this book will bring increased understanding and confidence to everyone facing the challenges of dealing with cognitive impairment linked to MS.

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1 What do cognitive difficulties mean for people with MS and their caregiver partners?

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This chapter briefly presents the voices of people with multiple sclerosis (PwMS) and their caregiver partners, the key stakeholders in our endeavors.

One woman's experience of multiple sclerosis (MS) with significant cognitive impairment, published as a journal article, includes her accounts of her difficulties:

> "When I am writing something, I stay focused, in the sense that I am not consciously thinking of anything else. Even so, it takes me at least five times as long as it did to produce what I want. Sometimes, if I do not look at the clock until I'm ready to stop, I'm floored by how much time has passed. I might think an hour has passed, but I've really been at it for three. And the writing process itself is a struggle in a way it never was. I start off knowing what I want to express. I use outlines, too. But when I have to start actually putting down my thoughts one word at a time, they somehow evaporate as soon as I start typing (or even using computer dictation equipment). The process used to be so fluid it felt like transcribing someone else's speech. Now I have lost that inner voice. I don't have the competence to describe what is happening with any greater precision, but … I hope you will understand what I mean."
>
> Anonymous and Stern, 2011[1]

Jeffrey Gingold is a PwMS and an award-winning author. In his book about facing the cognitive challenges of MS, he says:

> "Without warning, many people with MS are suddenly faced with an inability to process routine thoughts. Their decision-making may be stonewalled, befuddling simple conversations into a word-finding struggle. Others may lose their bearings in their own back-yard or kitchen, or suddenly the face of a spouse or friend will appear unfamiliar. Then, the shroud over their memory recall lifts, defying explanation, and leaving no trace of the bait and switch. The individual's cognitive functions have been

> compromised and often go undiagnosed, creating a deep chasm of hidden disability.”
>
> Gingold 2011[2]

Many PwMS experience frustration when cognitive difficulties reduce their daily functioning:

> “I find it annoying when I forget something.”
>
> Halstead et al., 2021[3]

> “I’m frustrated by the loss of my ability to read like I used to.”
>
> Halstead et al., 2021[3]

The support of a caregiver partner is of immeasurable value to a PwMS and is a key component of their wellbeing. Here is one account from a PwMS:

> “He’s like my external hard drive. He has to remember a lot of things for me … and I have trouble completing tasks, either because of exhaustion, because of pain, or because of my memory. So this combinations [sic] of things have put a burden on him.”
>
> Halstead et al., 2021[3]

Caregiver partners are also well aware of the personal impacts that cognitive difficulties can have on PwMS:

> “When she lost her job, she lost some of herself.”
>
> Halstead et al., 2021[3]

Healthcare professionals working with a PwMS and their caregiver partner are often engaging with a relationship that has recently settled at a new equilibrium so that the challenges being faced can be absorbed. Cognitive difficulties also often occur with a cluster of other related symptoms, which all need to be addressed for optimal outcomes. In the chapters that follow, we have tried to bring together the basic facts that support engagement, information, and actions that will enable MS clinics to optimally assess and manage cognitive difficulties.

Key points – what do cognitive difficulties mean for people with MS and their caregiver partners?

- Cognitive impairment causes pervasive and handicapping difficulties for PwMS.
- Caregiver partners are aware of the burdens and losses that cognitive impairment imposes on those they love.
- Caregiver partners provide major support for PwMS with cognitive difficulties.

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2 MS cognitive difficulties and their impacts

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‘Cognition’ is used as an umbrella term to describe any mental faculty, but is best described as the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses. Different domains of cognition are not equally affected by multiple sclerosis (MS).[1]

Domains of cognition vulnerable to MS

Information processing speed (IPS) is an indication of overall mental efficiency. Slowed IPS is the most common and pervasive cognitive deficit seen in people with multiple sclerosis (PwMS).[2] It can be thought of as ‘reduced bandwidth’. IPS underlies many other cognitive tasks and is thought by some to be the underlying difficulty that explains all cognitive deficits in PwMS. It is usually assessed by timed repetition of simple tasks.[2] PwMS with reduced IPS may find doing two things at once (for example, talking and walking) problematic, thus research in this area uses the dual-task paradigm.[3]

Memory encompasses the processes that are used to acquire, store, retain, and later retrieve information.[4] Memory difficulties are common in PwMS but are often mild.[5,6]

Verbal memory relates to any information presented and stored as words or digits (for example, conversations, personal identification numbers, and famous lines in films).

Visual memory refers to information that is presented and stored in a non-verbal format (for example, flags, maps, famous paintings, and car models).

Prospective memory is memory for intentions and enables us to remember to carry out an action that has been planned for a predefined time in the future (for example, taking tablets, attending appointments).[6,7] It is a complex function that involves attention, memory, and executive functions, and it may be that any one significant cognitive deficit may be sufficient to degrade prospective memory.[7] Difficulties with prospective memory can occur early in the disease[7] and may be disruptive to independence and relationships.[6]

Executive function is a set of mental skills that includes working memory, flexible thinking, and self-control, and executive dysfunction is common in PwMS.[8] We suggest thinking of executive functions as ‘cockpit skills’, in that they control, integrate, and ‘adjudicate’ between information arriving from other centers, and hence are involved in judgment and decision-making. They are also implicated in distractibility, which has been characterized as a form of disinhibition.[8]

Visuospatial processing is the ability to tell where objects are in space, including our own body parts. It also involves being able to tell how far objects are from us and from each other and having a sense of an object as a distinct physical entity (but not its name, which is a language skill). Our brains use visual coding for information that would be less efficiently managed verbally, such as flags, the faces of our friends and family, or recognizing cars or road signs. We use visuospatial processing skills for many tasks, from tying shoelaces to matching fabric or wallpaper patterns and reading maps. Visuospatial processing is hard to assess precisely in PwMS because of visual disturbances that are not considered ‘cognitive’ (such as nystagmus, acuity, and eye movements). As a result, it can be hard to tell whether a person is not ‘seeing’ the test materials well or is finding it hard to process the information more centrally.[9]

Language function is about communicating, expressing, and comprehending information in word form. The effects of MS on central language processing are usually less common than other cognitive deficits, but peripheral sensory and motor impairments can be considerable (for example, dysarthria and dysphonia).[10]

Social cognition describes a cluster of cognitive processes. Although they are most pronounced in older PwMS and those with other cognitive deficits, social cognition deficits can occur in the early stages of MS and may occur in isolation.[11] A common component deficit in PwMS is emotion perception, which makes it hard to detect, discriminate between, and interpret other people’s emotional states from facial cues. Also common is an impaired ability to attribute mental states (such as feelings, beliefs, intentions, and desires) to others, and to understand and predict others’ behaviors based on these imputed mental states (theory of mind).[12] The clinical relevance of these impairments is likely focused on the need for effective and adaptive social functioning, depending on the faculties involved, and may explain some of the interpersonal and employment challenges faced by PwMS. Interestingly, Montembeault et al. have reported that the reduced socioemotional sensitivity of PwMS does not appear to be observed by their relatives and caregiver partners.[12] This is surprising because a caregiver partner is usually accurate at reporting most aspects of their partner's cognitive status.

There are reports of PwMS being poor at picking up subtle inferences in social interactions. For example, they have been reported to be weaker at understanding sarcasm[13] and comprehending humor, either as a primary deficit or secondary to a more general comprehension deficit.[14] These tasks are sometimes characterized as 'pragmatic functions', requiring the integration of language and social context to infer the speaker's intended meaning. Several cognitive operations are involved in selecting and integrating relevant data from a context and associating them with general knowledge. It may be that PwMS fail to identify non-verbal cues and signals (for example, a raised eyebrow or a doubtful expression), which are essential to understanding a chain of events.[15]

Prevalence of cognitive deficits by domain

Although on an individual basis there is high variability of cognitive status, in large groups of PwMS, IPS and learning and memory are most often affected, while executive function and visuospatial processing are less frequently involved. In one study of 291 adults with MS, the prevalence of impaired domains (varying by test) was 27–51% for IPS, 54–56% for visual memory, 29–34% for verbal memory, 15–28% for executive function, and 22% for visuospatial processing. Much rarer deficits were language, semantic memory, and simple attention span (each about 10% prevalence).[1]

Effects of cognitive deficits

Studies have shown that cognitive deficits in PwMS have a significant and measurable impact on many aspects of a person's life, and this is clear even when other possible explanatory factors (such as physical disability, depression, and fatigue) are accounted for. It is very important that MS clinic staff know how best to tackle these issues and support PwMS.

Quality of life. Cognitive difficulties can have negative impacts additional to those imposed by physical impairments.[16] Taking a general view, it is known that cognitive difficulties adversely affect quality of life (QoL), which is not merely the absence of disease, but physical, mental, and social wellbeing. The effects of cognitive impairment in MS can be wide ranging, pervasive, and disabling. Not surprisingly, their impact on QoL is well documented.[17]

Disease management. Perhaps most importantly for the MS clinic, cognitive difficulties can affect how well PwMS manage their disease. They are confronted by considerable challenges when deciding between therapies with complex risk/benefit profiles. Medical decision-making capacity is characterized as having five measurable consent standards:[18]

- expressing a treatment choice
- making a treatment choice
- appreciating the risks/benefits of a choice
- reasoning about a choice
- understanding the disease and treatment options.

In one study, vignettes about a disease and possible treatments were presented to people with progressive MS and healthy control participants, with both groups also completing a cognitive assessment. Appreciation, reasoning, and understanding were worse for PwMS than healthy controls, and correlated with their working memory, verbal memory, and verbal fluency scores.[18] This indicates that cognitive deficits reduce how well PwMS are able to participate in medical decision-making.

To assess the impact of impaired cognition on adherence to disease-modifying treatment (DMT), an 8-week study collected adherence data for a DMT injected daily via self-report forms, medication diaries, and needle disposal. Among other factors, scores on baseline objective tests of memory correlated with all adherence measures,[19] indicating that PwMS with objective memory difficulties are at increased risk of poor DMT adherence. Interestingly, another study has reported that PwMS often cite memory difficulties as a reason for poor adherence.[20] IPS has

TABLE 2.1

Significant factors that predict non-adherence to DMT in PwMS

	Adherent/non-adherent				
Variable	**β**	**SE**	**Odds ratio**	**95% CI**	***P*-value**
SDMT score	0.097	0.031	1.10	1.04, 1.17	<0.05
Self-injected drug	1.534	0.646	4.64	1.31, 16.46	<0.05
Duration of treatment	1.624	0.751	5.07	1.16, 22.10	<0.05
EDSS score	0.816	0.347	2.26	1.14, 4.46	<0.05

Results of binary logistic regression analysis for factors for predicting medication adherence. CI, confidence interval; EDSS, Expanded Disability Status Scale; SDMT, Symbol Digit Modalities Test; SE, standard error. Reproduced with permission under the terms of the Creative Commons Attribution 4.0 International (CC BY 4.0) license from Giedraitiene et al., 2022.[21]

recently been reported to be the variable most closely associated with adherence (Table 2.1).[21]

Engagement with rehabilitation and its potential benefits are also compromised by cognitive deficits. PwMS with poor verbal learning skills are more likely to miss physiotherapy appointments, and reduced working memory and IPS mean PwMS are less likely to meet physiotherapy rehabilitation goals.[22] Verbal intelligence also affects multidisciplinary rehabilitation outcomes, even when baseline physical disability is accounted for.[23]

Safety. Unsurprisingly, cognitive impairment means that PwMS are statistically less safe than people who do not have MS.

Risk of falls. A study comparing PwMS divided into groups of fallers and non-fallers demonstrated that the fallers were worse on all cognitive measures.[24] This has been attributed to cognitive–motor interference, where reduced IPS means less processing capacity can be devoted to postural control.[25]

Driving requires the coordination of multiple sensory and cognitive functions, such as vision and attention.[26] Around one-fifth of drivers with MS fail driving assessments on the road. Detailed studies have reported that these failures are linked to stimuli errors, errors in judging spaces in traffic, and strategic errors in all settings in the context of low physical disability levels. A combination of peripheral visual acuity and more central cognitive skills (such as central visual processing speed, visual information processing, and immediate and delayed visual recall) has been linked to these errors. In one driving simulator study, PwMS and healthy control participants 'drove' through three scenarios. Immediate verbal/auditory recall (assessed by a verbal learning test) and divided attention and visual processing speed (measured by identifying a car or truck in the center of a screen while concurrently identifying the location of a peripheral object) were linked with 'driving' performance. The following results were observed:

- a sudden traffic light change, where PwMS were less likely to stop
- a pedestrian stepping out in front of the car just as the driver was told to turn right, where PwMS had slower response times
- a navigational task in an urban environment, to be completed by following road signs, where there was no difference between groups.[26]

One study compared driving violations from a court database for PwMS with those of matched healthy participants. PwMS had a greater number of driving violations and were weaker on a number of cognitive tasks, including visuospatial skills, learning, and executive functioning.[27] Another comparison of PwMS with cognitive impairment, PwMS without cognitive impairment, and healthy control participants showed that PwMS with cognitive impairment had been involved in more motor vehicle crashes.[28]

Financial affairs. A systematic review identified three studies of the financial management skills of PwMS, and all three concluded that they faced some difficulties compared with healthy controls. Impaired financial decision-making was shown to correlate with a range of cognitive deficits (IPS, language, memory, arithmetic skills, and executive functions, such as mental flexibility, working memory, and verbal reasoning); however, in one study, IPS was the only significant predictor of total money management score.[29]

Employment. Unsurprisingly, impairments in a number of cognitive domains have been linked to reduced employment (Figure 2.1).[30,31] One systematic review, which identified 19 studies, concluded that

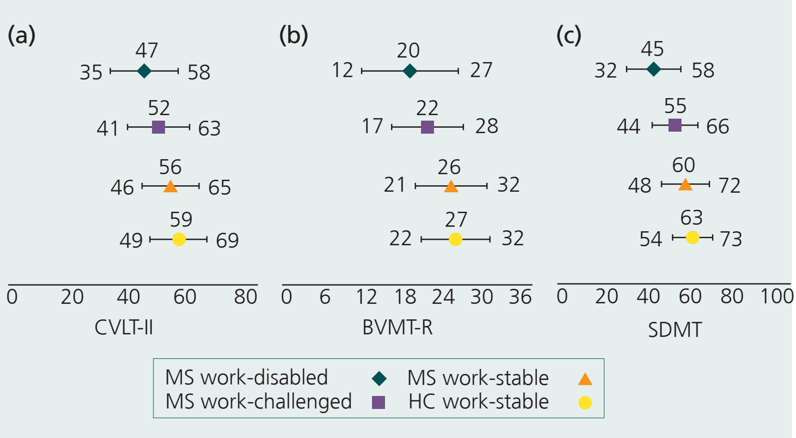

Figure 2.1 Cognitive tests of (a) verbal memory (CVLT-II), (b) visual memory (BVMT-R) and (c) IPS (SDMT) each produced mean scores that differed significantly between patients with MS and healthy participants ($p < 0.001$): HC work-stable, healthy participants at work; MS work-stable, PwMS who were work stable; MS work-challenged, PwMS who were work challenged; MS work-disabled, PwMS who were work disabled. BVMT-R, Brief Visuospatial Memory Test-revised; CVLT-II, California Verbal Learning Test Second Edition; SDMT, Symbol Digit Modalities Test. Reproduced with permission from Benedict et al., 2016.[31]

increased work disability was associated with reduced cognitive function (and increased physical disability).[32] IPS has also been shown to be an independent predictor of income, even after correction for clinical and sociodemographic variables, including physical disability,[33] with one study showing that weakening of IPS or verbal memory was independently linked to reduced employment status (unemployment or transition from full- to part-time work) over several years.[34]

Participation is defined as ‘involvement in a life situation’. Although participation is determined multifactorially, there is evidence that cognitive status is a significant predictor of participation in activities of daily living, such as leisure, social, and religious activities.[35] Cognitive disorders have been found to be more closely associated with participation restrictions than physical disorders for

PwMS,[36] and IPS has been reported to be an independent predictor of sustained participation over a 10-year period.[37]

Specific aspects of social interaction difficulties have been linked to cognitive deficits, and the compromised social cognition skills of PwMS may negatively affect employment and participation. IPS is related to PwMS' social support levels, in that weaker IPS is linked to reduced social support.[38] One study found that PwMS with reduced emotion perception have weaker social functioning and report less social support from their friends.[39]

PwMS with weak social cognition skills have been particularly challenged by the coronavirus disease 2019 (COVID-19) pandemic. For example, the recognition of emotions on faces wearing masks has been shown to be harder for PwMS than for healthy controls.[40]

Caregiver partners. Supporting a PwMS with cognitive difficulties is a major and far-reaching burden. The severity of the cognitive problems of a PwMS, as reported by their caregiver partner, is associated with the extent of strain[41] and worse health-related QoL experienced by caregiver partners. Only one cognitive test for PwMS, of IPS, was individually related to caregiver partner health-related QoL.[42] Some indication of the burden of caring for a family member with MS can be found in the results of a qualitative study which investigated the impact of cognitive impairments on adults with MS and their caregivers.[43] The study highlighted six key areas where the cognitive impairments of MS affected the lives of the PwMS and their caregiver partner:

- social impact of cognitive impairment in MS
- changes to daily living
- relationship quality
- communication
- coping with MS
- desire for help to manage MS.[43]

Pediatric-onset MS

Although much rarer than adult-onset MS, there is increasing interest in and understanding of pediatric-onset MS (POMS).[44] Cognitive assessment of patients with POMS can be challenging because of differing age- and sex-related developmental trajectories, which require comparison with different normative groups. Like adult PwMS, IPS, attention, verbal and visuospatial memory, and executive functions are most frequently affected in studies comparing patients with POMS with age-matched healthy control participants. However, patients with POMS may also have weaker language skills and lower levels of general intelligence than age-matched healthy control participants, which are not demonstrated in studies of adult MS cognition.[45]

Key points – MS cognitive difficulties and their impacts

- Cognitive dysfunction has a major negative impact on PwMS and can affect their QoL, disease management, safety, ability to manage their financial affairs effectively, employment, and participation.
- IPS and memory difficulties are the most common cognitive impairments in PwMS. Problems with executive dysfunction, language, and visuospatial function are less common.
- PwMS can also have difficulties with emotion perception, causing them to struggle to anticipate and understand the emotional states of others. This can disrupt relationships, employment, and other aspects of participation.
- As well as impacting PwMS themselves, cognitive deficits can also diminish the health-related QoL of their caregiver partners.

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3 How do MS cognitive deficits relate to other variables?

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Variables

Disease phenotype

Radiologically isolated syndrome and clinically isolated syndrome. Radiologically isolated syndrome (RIS) occurs when a person is discovered by chance to have lesions on an MRI scan that would be consistent with multiple sclerosis (MS), but they have experienced no clinical symptoms. Clinically isolated syndrome (CIS) is diagnosed when a person has a first episode of neurological symptoms that lasts at least 24 hours and is caused by inflammation or demyelination (loss of the myelin that covers the nerve cells) in the CNS. It may often lead to MS over time, but alone is not enough for a diagnosis of MS to be made.[1]

Few studies of cognitive deficits in RIS are available, so prevalence has not yet been determined. Across studies, cognitive impairments have been detected in 12–57% of patients with CIS, defined as scoring below the normal range on at least two tests. The pattern in people with CIS usually involves reduced information processing speed (IPS) and difficulties with verbal and visual memory; however, executive function, including verbal fluency, can also be impaired.[2]

Relapsing remitting multiple sclerosis. In a study of patients with early relapsing remitting MS (RRMS) at community neurology practices, 45% were found to be cognitively impaired. The pattern of cognitive deficits in people with RRMS is similar to that of people with CIS, mainly involving IPS and verbal and visual memory, and sometimes verbal fluency.[2]

Secondary progressive multiple sclerosis (SPMS) is associated with a greater frequency and severity of cognitive deficits than RRMS. A high prevalence of cognitive deficits has been reported for people with SPMS, ranging between 56% and 80%.[2] More severe impairment in IPS, episodic verbal memory, working memory, and verbal fluency has been demonstrated in patients with SPMS than those with RRMS.[3] A wider range of domains also appears to be affected in individual patients.[2]

Primary progressive multiple sclerosis. Over the past two decades, a number of studies have demonstrated cognitive impairment prevalence rates of up to 90% in this population.[3]

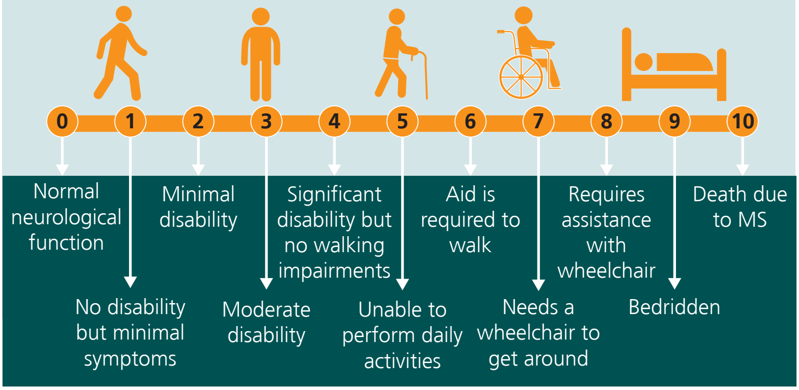

Figure 3.1 The EDSS is used to track disability progression of PwMS.[4]

Physical disability, as rated by the Expanded Disability Status Scale (EDSS) (Figure 3.1),[4] is moderately associated with cognition in people with MS (PwMS). In one study, EDSS correlated significantly with IPS ($r=-0.55$, $p<0.01$), visuospatial memory ($r=-0.54$, $p<0.01$), and verbal memory ($r=-0.40$, $p<0.05$).[5] However, there are variants of MS where cognition and EDSS are less aligned. In one study, stable, low EDSS scores were recorded for people with supposedly ‘benign’ MS while cognitive impairments accrued. After 15 years, EDSS-based assessment indicated a prevalence of remaining benign MS of 23% of the study population, while assessment of cognition reduced it to 16%.[6] Similarly, presentation of so-called ‘cognitive MS’ is sometimes recorded, although it is rare, where significant cognitive and/or psychiatric symptoms are the main presenting features in the context of little or no physical disability.[7]

Clinical MRI findings are only mildly related to cognitive function in PwMS. A systematic review and meta-analysis calculated an aggregate correlation between cognition and T2 lesion burden of only $r=-0.30$ (95% CI: –0.34, –0.26).[8]

Aging. Cognitive impairment is more common in older PwMS than their healthy peers. Of PwMS aged 55 years and over, 77% have been reported to demonstrate impairment in two or more cognitive domains. In a comparison of PwMS who first developed symptoms before age 40 years with those who developed symptoms later, the later-onset group had worse visual and working memory than the younger-onset group, although IPS and verbal memory deficits were similar. It may be that disease progression in older PwMS is exacerbated by age-related changes in the brain.[9]

Fatigue. Up to 80% of PwMS report fatigue during their disease course, and some describe it as one of the worst symptoms. Many PwMS report that fatigue affects their cognitive function; however, reports of fatigue often do not relate to objective cognitive test scores.[10] Sustained-attention cognitive tasks seem to be the most affected by fatigue.[11]

Mood disorders. Depression is more common in PwMS than in the general population. A population-based Swedish study reported a prevalence of depression of 19% in PwMS (compared with 4–10% in the general population).[12] The lifetime risk of a diagnosis of depression is up to 50% for a PwMS.[13]

Many PwMS who are depressed or anxious report cognitive deficits; however, studies of the effect of mood disturbance in PwMS assessed by objective cognitive tests have been inconsistent, often showing that they are not related.[14] In one large study, anxiety symptoms were associated with slower IPS and reduced verbal learning skills, but baseline depressive symptoms were not.[15] However, changes in mood over the course of the study had opposing effects. Changes in anxiety symptoms did not affect cognitive test scores, whereas changes in depressive symptomology had modest effects on objective test scores, but not enough to be clinically meaningful.

Notably for PwMS with early disease and minimal disability, depression had a more pronounced negative effect on multitasking than monotasking (traditional single-domain tests), an effect that was not seen for healthy controls.[16] It may be that patients are able to adequately perform a single task in a quiet room (conventional testing), but are less competent in real-life settings with distractions, which overwhelm their central processing, as a result of both reduced IPS and depression.

Reduced processing capacity. In addition to the effects on multitasking described above, the effects of reduced IPS on overall processing capacity also impair dual-task performance of PwMS. This can impair the ability of a PwMS to perform gait/balance and cognitive tasks concurrently, which is attributed to cognitive–motor interference.[17]

Change in cognitive impairment over time. Many PwMS may remain cognitively stable for a few years.[18] However, over a decade or more, cognitive dysfunction is likely to emerge and progress in a sizable proportion of patients. In one study, 74% of patients were free of cognitive impairment at the start, but this had fallen to 44% after 10 years.[19] Numbers of patients with mild or moderate impairment increased over the same period. Several subsequent larger studies have shown a significant relationship between cognitive impairment and disease duration.[2]

Evidence from longitudinal studies indicates that there is a staging of cognitive impairments in MS in the following order: IPS, visual learning, verbal learning, working memory, and executive function.[20] These stages have been linked to physical disability and employment changes.

Diverse neuroimaging parameters (global or regional changes, lesion-based or non-lesion analyses, and grey- or white-matter volume, the last two being unavailable in most clinics) are related to future cognitive deterioration. In a pooled analysis, they were medium predictors of cognitive decline ($r=0.47$).[21,22]

Cognitive reserve (CR) can be thought of as the dynamic availability of cerebral resources to sustain function. People with greater premorbid CR are better able to maintain cognition despite disease progression and it can be used to predict future deterioration. In a convincing prospective longitudinal study, PwMS were followed for 4.5 years. Those with greater premorbid intellectual enrichment experienced less IPS and memory decline.[23,24]

Future disease course. If cognitive dysfunction is present at RRMS diagnosis, the chance of the PwMS reaching EDSS 4.0 is three times greater (hazard ratio [HR]=3.18, $p<0.001$) than if it is not present, and conversion to SPMS is more than twice as likely (HR=2.54, $p=0.008$) over the next 10 years. Better verbal memory scores and IPS are linked to lower SPMS conversion rates.[25] In a large retrospective study of PwMS, cognitive dysfunction was associated with increased risk of death (adjusted HR = 3.07, $p = 0.006$) and the association was strongest for those with a progressive disease course (Figure 3.2).[26] The association between cognitive dysfunction and worse clinical

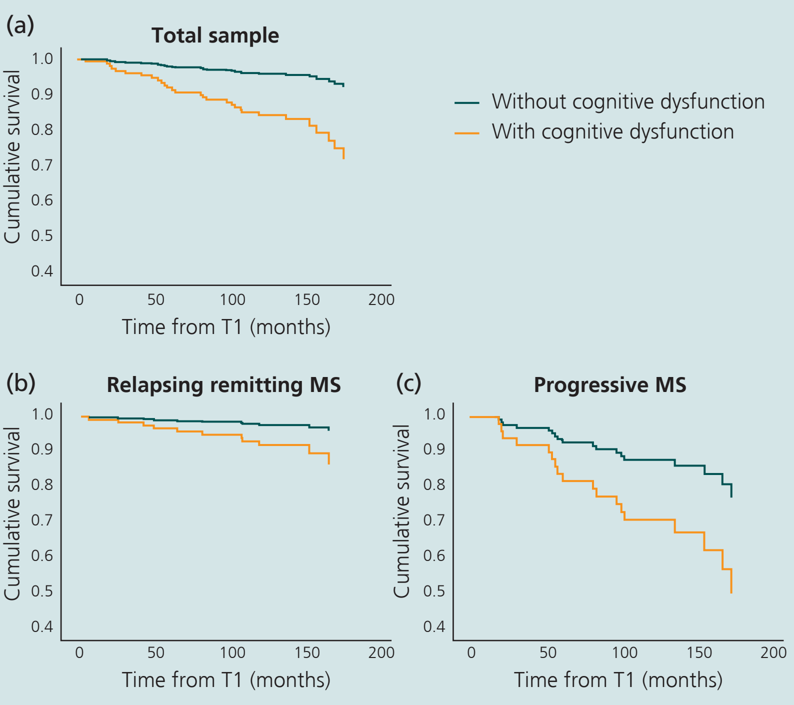

Figure 3.2 Survival curves according to cognitive assessment performance for (a) the total sample of PwMS, (b) the relapsing remitting course subgroup, and (c) the progressive disease course subgroup. Of the total sample of 408 PwMS at study entry, 77 had cognitive dysfunction and 322 had RRMS. Reproduced with permission from Cavaco et al., 2022.[26]

outcomes and mortality may signify more widespread neuropathology, and reflect the impact of comorbidities and lifestyle features.

Pediatric-onset MS. Cognitive dysfunction is consistently reported to affect one-third of pediatric patients with MS; however, the use of different test batteries across studies and the lack of a consensus definition for cognitive impairment have meant that different patterns of impairment have been reported. There is also the methodological challenge in longitudinal studies that the healthy control group must be matched precisely for age and will change over time, following a normal developmental trajectory. As in PwMS with adult-onset disease, reductions in IPS, verbal and visual memory, and executive functions are most frequently reported. However, language skills and general intelligence have also been shown to be reduced in children. Failure of age-expected brain growth in pediatric patients with MS is likely to be linked to cognitive dysfunction, but the relationship has not yet been clearly elucidated.[27] The few studies to date that have investigated CR in pediatric PwMS suggest a protective role, especially in the early stages of disease.[28]

Key points – how do MS cognitive deficits relate to other variables?

- Small studies of RIS and CIS have demonstrated cognitive impairment in some patients, even at early stages, with IPS and memory mainly affected.
- When present in CIS, cognitive impairment is similar to that of people with RRMS, mainly involving IPS and verbal and visual memory, and sometimes verbal fluency.
- Progressive MS phenotypes tend to experience more severe and more widespread cognitive deficits.
- Cognitive dysfunction is only moderately related to disease variables such as EDSS and MRI findings.
- Cognitive impairment in the early stages of MS is related to worse disease outcomes.

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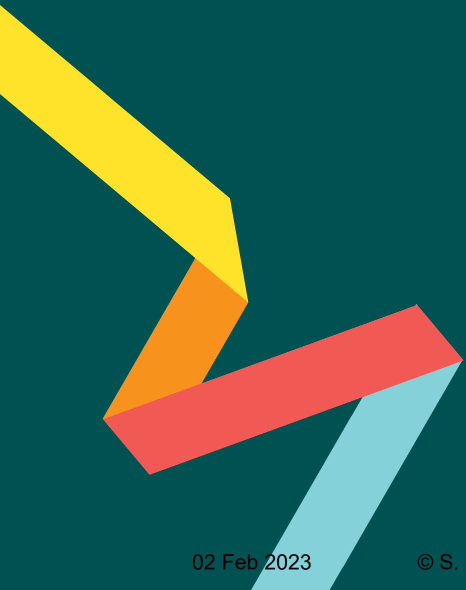
4 Assessment strategies



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The importance of formal cognitive assessment

The number of people with multiple sclerosis (PwMS) undergoing cognitive assessment is increasing,[1] but most PwMS around the world do not get the benefit of formal cognitive assessment. This is despite many peer-reviewed papers in neurology journals advising that formal cognitive assessment should take place at diagnosis and each year thereafter. Some of the most comprehensive recommendations for cognitive screening and management have been produced by a panel convened and funded by the US National Multiple Sclerosis Society, and endorsed by the Consortium of Multiple Sclerosis Centers and the International Multiple Sclerosis Cognition Society.[2] Formal cognitive assessment is recommended for several reasons.

Informal assessment is unreliable. Determining whether a PwMS has a cognitive impairment on an informal basis is not very reliable and healthcare professionals (HCPs) judging cognitive status on the basis of a routine consultation are often wrong (in fact, one study found that neurologists' accuracy when judging the presence or absence of cognitive impairment was not significantly different from chance).[3] This may be because language skills remain largely intact in PwMS, therefore conversation appears normal. However, the ability to hold a normal conversation is not necessarily backed up by intact memory and reasoning skills.

Self-reporting of cognition by PwMS may be inaccurate and may not relate closely (or sometimes even at all) to their objective test scores. A person's evaluation of their own cognitive status is influenced by mood, fatigue, and other psychosocial factors, and the responses of PwMS to surveys and questionnaires about money management, social interaction, everyday activities, and problem solving have all been shown to be influenced by mood.[4] Although an understanding of the PwMS' experience of cognition is fundamental to the therapeutic relationship, precise indication of their cognitive function is essential for optimal management. Thus, if clinical observation or observations by family and friends suggest the possibility of cognitive impairment, comprehensive assessment including cognition is required, even if the PwMS attributes the issue to depression, fatigue, or reduced mobility.[5] Self-reporting of cognitive status can be evaluated using the Multiple Sclerosis Neuropsychology Questionnaire (MSNQ) – Patient tool.[5]

Importantly, a caregiver partner's account of the cognitive status of a PwMS is often aligned with their objective test scores.[6] This is why it is essential to get a relative's account of a PwMS' cognitive function. The validated MSNQ – Informant tool can be used to capture a caregiver partner's perception of the PwMS' cognitive status.[7]

Objective cognitive tests

A recent review identified 5665 different measures of cognition used in published studies of multiple sclerosis (MS) cognitive functioning.[8] Despite this high number, there are three batteries in widespread research and clinical use:[9]

- Brief Repeatable Battery of Neuropsychological Tests (BRB-N)[10]
- Minimal Assessment of Cognitive Function in MS (MACFIMS)[11]
- Brief International Cognitive Assessment for MS (BICAMS).[12]

Each battery aims to assess multiple domains of cognitive function, and they vary in duration and the level of expertise required by the assessor (Table 4.1). The MACFIMS and BRB-N can only be used by psychologists,[9] and considerable resources are required to buy, store, and devote time to administering and scoring them.[12] If time is at a premium, use of the Symbol Digit Modalities Test (SDMT) alone gives a useful indication of cognitive status and takes 5 minutes to administer.[12] A number of computerized cognitive tests have been developed for MS, but have undergone limited validation to date and may require the patient to be in the clinic to complete them, attended by a technician.[13]

BICAMS has strong psychometric properties and is the only cognitive battery that is widely recommended for routine MS clinic assessment.[9] It takes 15 minutes to complete and can be performed by most HCPs[12] (see Table 4.2 for practical guidance on how to conduct cognitive testing with BICAMS). The components of BICAMS are outlined below.[14]

- The SDMT involves a simple substitution task. Using a reference key, a patient has 90 seconds to pair specific numbers with given geometric figures. Responses are spoken.
- California Verbal Learning Test Second Edition (CVLT-II) learning trials. There are five trials. In each trial, a list of 16 items is read

aloud to the patient, who must recall as many as they can. Responses are spoken.

- Brief Visuospatial Memory Test-Revised (BVMT-R) learning trials. In each trial, the array of six geometric figures is displayed for 10 seconds, then removed. The patient must draw the array. There are three trials.

TABLE 4.1

Comparison of the three main batteries for testing cognition in PwMS

Cognitive domain	BRB-N[9,10,12]	MACFIMS[9,11]	BICAMS[12]
Information processing speed	SDMT	SDMT	SDMT
Working memory	PASAT 2s, PASAT 3s	PASAT 2s, PASAT 3s	N/A
Verbal memory	SRT	CVLT-II	CVLT-II learning trials
Visual memory	SPART (10/36)	BVMT-R	BVMT-R learning trials
Executive function	N/A	D-KEFS sort	N/A
Verbal fluency	WLG	WLG	N/A
Spatial processing	N/A	JLO	N/A
Time needed for administration	45 mins	90 mins	15 mins
Level of administration expertise required	Moderate skill required,[†] only accessible to psychologists	Significant skill required,[†] only accessible to psychologists	Minor skill required, recommended for most HCPs
International validation/norms*	7	6	30

*Numbers identified by PubMed search in July 2022 using '(TEST)' validation.

[†] Based on authors' experience. BVMT-R, Brief Visuospatial Memory Test-Revised; CVLT-II, California Verbal Learning Test Second Edition; D-KEFS sort, Delis–Kaplan Executive Function System conceptual sorting task; JLO, Judgment of Line Orientation; N/A, not applicable; PASAT 2s/3s, paced auditory serial addition test, 2-second/3-second presentation; 10/36 SPART, 10/36 Spatial Recall Test; SRT, Selective Reminding Test; WLG, word list generation.

TABLE 4.2

Procedure for BICAMS cognitive assessment

Patient should have completed fatigue and mood scale assessments recently; if not, include them in the assessment

Ensure all components required are present before the assessment begins and that you are practiced in their use (instructions for administration can be found in the test manuals; it is essential that they are followed and scoring conducted exactly as specified, otherwise the results are not valid)

The examiner will need:

- Pen
- Stopwatch
- SDMT sheet to record patient's spoken responses
- SDMT instructions
- CVLT-II learning trials form with word list printed five times, instructions, and space to record patient's five recall attempts
- BVMT-R instructions

The patient will need:

- Pencil with eraser on the end
- SDMT key
- BVMT-R template array
- Three blank sheets of A4 white paper labeled T1, T2, and T3 for BVMT-R drawing trials

Arrange to see the patient alone in a quiet room, and sit across the table from them

BICAMS is as sensitive to cognitive impairment as the 'gold standard' 90-minute MACFIMS battery.[15] By also including memory scales, BICAMS captures a broader range of skills than the SDMT alone. There is evidence that the SDMT may not change much in progressive MS and is only moderately and weakly correlated with visuospatial and verbal memory, respectively.[16] This means that although the SDMT alone can give definite positive identification of cognitive impairment, use of the SDMT alone may miss memory difficulties, if they are present.

BICAMS has an international validation protocol.[14] At the time of writing, 26 countries had published national validations, confirming the psychometric properties of BICAMS across different cultures and language groups.[17] BICAMS is in use in a number of international treatment trials[14] and, at the time of writing, 130 studies had been published that used it to investigate MS cognition, demonstrating the further validity of BICAMS in relation to physical disability and brain pathology (criterion validity), and everyday functioning including employment (ecological and external validity).[14,18–20] Adding BICAMS to routine Expanded Disability Status Scale (EDSS) assessment for PwMS with EDSS 4.0 or lower identified a further 25% of the PwMS studied as having cognitive impairment. These people had been missed by assessment by EDSS alone.[21] Sensorimotor dysfunction may be a confounder of test performance (for example, poor upper limb function or vision, or dysarthria).[22]

Annual cognitive assessment with BICAMS is recommended.[12]

Assessment in the MS clinic

In a recent survey of US MS clinics, 53% reported no formal procedure for objective assessment of cognition in PwMS; 33% of clinics reported using an assessment such as the SDMT, up from 21% reported 10 years previously.[23] There is growing awareness that formal cognitive assessment constitutes best practice[23] and PwMS are generally very positive and accepting of routine cognitive assessment.[24] Once mood and fatigue scales have been completed, and identified issues addressed if appropriate, and a subsequent cognitive assessment has been completed, MS clinic staff will know with some certainty whether primary cognitive impairment is present and will be able to instigate appropriate management strategies for cognition.

For suggestions and guidance relating to structuring and presenting information about cognition and testing, see Chapter 8 ‘Difficult conversations’.

Key points – assessment strategies

- Formal cognitive assessment is the only valid and reliable way to evaluate whether a PwMS has a cognitive impairment.
- Caregiver partners will often give a cognitive status report for a PwMS that is closer to that individual's objective test scores than to the PwMS' evaluation of their own cognitive status. This can be useful in assessment and monitoring (for example, MSNQ – Informant questionnaire).
- The three most recognized cognitive batteries in MS are the MACFIMS, BRB-N, and BICAMS.
- BICAMS has good psychometric properties and is the only MS cognition battery recommended for routine clinical cognitive assessment. It can be administered by any HCP in about 15 minutes and has been validated in many countries.

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5 MS clinic management of cognition I: healthcare professional information and action

HEALTHCARE

This chapter focuses on information and actions for healthcare professionals (HCPs) working in the multiple sclerosis (MS) clinic. It assumes that the Brief International Cognitive Assessment for MS (BICAMS) has been completed and has demonstrated that a person with MS (PwMS) has cognitive impairment.[1] In this common situation, the multidisciplinary team will know that cognitive impairment is present but will not yet have a detailed cognitive profile of the patient to inform their work.

Clinic cognition audit

We recommend that a clinic cognition audit for MS (CCAMS) should be completed annually for every patient with MS, regardless of their known cognitive status; if cognitive impairment has been demonstrated, this should become a priority. It is helpful to keep a systematic record of the audit, actions, and advice given, with review dates noted. Figure 5.1 provides a template for such a record.

Disease-modifying treatments

Protective effects. A recent systematic review has suggested that disease-modifying treatments (DMTs) offer some protection for cognition, in relapsing remitting MS (RRMS) at least, although the majority of the studies included were observational (and thus had weaker experimental design to determine outcomes).[4] In addition, a large observational study using retrospective chart review has suggested that the slowing of the physical progression of MS by DMTs may be accompanied by a slowing of cognitive deterioration.[5] If progression of the underlying disease pathology is slowed, it seems probable that cognitive decline may be reduced.

To our knowledge, none of the 19 DMTs licensed for MS in the UK has any cognitive indications on the label for starting or escalating treatment. Despite a lack of formal DMT guidance regarding cognitive progression and treatment escalation, cognitive progression may be considered a cue to investigate other aspects of MS that can indicate that treatment escalation is required.[6] There is no convincing evidence that any symptomatic medication improves cognition in MS (including acetylcholine esterase inhibitors, CNS stimulants, fampridine, and herbal remedies).[7]

Name or hospital label		**NHS/hospital number**	**DOB**	**Date(s)**
				First assessment
				Review
Topic	**Recommended**	**Action**	**Review**	**Further information**
Clinic cognitive assessment	If appropriate, manage fatigue and/or mood, assessed by: Fatigue scale (NFI-MS) Mood (HADS) Cognition (BICAMS)			
DMT optimal? Adherence?	Review efficacy, objective cognitive change, DMT adherence, DMT risk-monitoring adherence; consider escalation			
Symptomatic medications optimal? Adherence?	Review medications with adverse effects on cognition (e.g. anticholinergics)			
Comorbidities well managed?	Review diabetes, cardiovascular monitoring, cancer care			
Brain health: advice and adherence?	Review lifestyle (sleep, diet, exercise, smoking, alcohol, mental activity, self-prescribed/recreational drugs)			
HCP interaction style to support cognition	Quiet room without distractions, speak slowly, simple grammar, use high-frequency words, check understanding, ask patient to repeat key points when summing up			

BICAMS, Brief International Cognitive Assessment for MS; HADS, Hospital Anxiety and Depression Scale;[2] NFI-MS, Neurological Fatigue Index – Multiple Sclerosis.[3]

Figure 5.1 Suggested template for conducting an annual CCAMS for a PwMS.

Side effects. The likelihood of any cognitive impairment being linked to a serious, acute DMT side effect should be considered. For example, progressive multifocal leukoencephalopathy (PML) is a viral disease characterized by progressive damage or inflammation of the cerebral white matter that can occur in PwMS. There are cases on record of PML being linked to DMTs, including natalizumab.[8] PwMS in these medical circumstances often present with cognitive changes and may experience cognitive losses due to PML. It has been reported that 'atypical' cognitive deficits in MS may support the early diagnosis of PML.[8] However, the relative lack of specificity in neurological symptoms related to PML means that new focal deficits may be misinterpreted as a MS relapse, resulting in delayed diagnosis of PML.[9] Urgent expert medical advice should be sought, should any suspicion of PML arise.

There may be a cognitive rebound after a high-efficacy therapy is discontinued.[10] Several studies have demonstrated that discontinuation of natalizumab is associated with a high risk of clinical and radiological disease reactivation. One study showed that 1 year after discontinuing natalizumab PwMS had returned to the level of cognitive impairment experienced before treatment started.[10]

Adherence should be explored, monitored, and supported as required. It is important to take into account the increased risk of poor DMT adherence in the context of cognitive impairment, and patients' understanding relating to DMT risk management and monitoring may also be compromised and require extra support (prompts for appointments, reminder phone calls regarding red-flag symptoms etc.).

Management of other symptoms

If the CCAMS protocol has been followed (see Figure 5.1), mood and/or fatigue will have been managed (if appropriate) before cognition is addressed. Management of other symptoms in PwMS should be reviewed regularly, because poorly managed or new symptoms may adversely affect cognition. An infection (for example, a urinary tract or chest infection) can make a PwMS appear confused.[11] Pain and pain medications can interfere with concentration. In addition, medication prescribed to manage symptoms may adversely affect cognition.[12,13] One case-controlled study, although a weak design to evaluate outcomes, suggested that some anticholinergics prescribed for bladder dysfunction adversely impacted cognitive function.[14]

Sleep disturbances are common in PwMS and occur about four times as often as in the general population. The most frequent primary sleep problems include insomnia, restless leg syndrome, sleep-related movement disorders, and sleep-disordered breathing.[15] Sleep disturbances have been linked to cognitive difficulties in PwMS,[16] even early in the disease.[17] Lifestyle changes and sleep hygiene can be effective management strategies.[18]

Other comorbidities. It has been estimated that around 50% of PwMS live with vascular comorbidity (including diabetes, hypertension, hyperlipidemia, and ischemic heart disease) and incidence is rising.[19,20] It is important to consider vascular comorbidities in the management of cognitive difficulties, because they are known to contribute to MS disease outcomes, are likely to contribute to cognitive impairment,[20] and are potentially modifiable.

A large retrospective chart review of PwMS reported that those with one or more comorbidities at baseline were slower on a test of information processing speed (IPS).[21] IPS decreased more steeply over 4 years for PwMS with two or more comorbidities than those with none. In fact, even the Framingham risk score, which calculates a 10-year probability of developing macrovascular disease, correlated with verbal learning dysfunction in PwMS.[22]

Taken together, the evidence suggests that cardiovascular conditions and even precursor cardiovascular risks should be carefully managed to protect cognition. It is also worth noting that neurological comorbidities, such as epilepsy, and the medications used to treat them may adversely affect cognition.[23]

The Brain Health initiative

Cognitive reserve (CR) as a concept was introduced in Chapter 3. Just as comorbidities deplete CR, lifestyle factors have been identified that protect it. It is now well established that positive lifestyle choices can slow the progression of MS, most of which have also been shown to slow cognitive decline. In a large online survey that relied on less-dependable self-reported cognitive function, greater cognitive impairment was linked to smoking and higher body mass index, while physical activity and a good-quality diet were related to less cognitive impairment.[24] A good summary of the Brain Health approach is outlined in a paper by Brandstadter et al.[25] MS Brain Health (msbrainhealth.org) provides extensive information for HCPs.

Alongside the established list of lifestyle choices that slow the progression of MS, there is an additional special strategy for cognition. Given the evidence for CR (see Chapter 3) and its protective value against disability in the general population,[26] it is likely that regular mental exertion can preserve or build up CR, protecting cognition in PwMS.[27] For example, reading a book is good for CR, joining a book discussion group is better and writing a short story is best. Similarly, playing an instrument is good for CR, learning a new piece of music is better, and playing the new piece from memory is best. From the Alzheimer disease protection literature, learning a new language seems to be very good.[28] It has been suggested that psychosocial factors, such as perceived control, religious activity, and social networks, may also contribute to CR.[29]

MS clinic staff should take a holistic stance to protecting cognition and ensure that medication, monitoring, and advice is always optimal from the perspective of cognition. Some opinion leaders believe a wide range of modifiable factors contribute to disease progression and should legitimately be routinely considered and addressed by MS clinics (Table 5.1).[30]

Recreational drugs have been shown to have a negative effect on cognition in PwMS and this should be fully discussed with patients who are using cannabis or other recreational drugs, so that they can make an informed choice. A comparison of PwMS using cannabis several times a week with non-users demonstrated worse IPS and spatial memory in the user group.[31] However, it appears that even long-term cannabis users can show significant improvements in cognition after just 28 days of cannabis abstinence.[32] This may be useful evidence to share with patients.

Pediatric-onset multiple sclerosis. It can be challenging to encourage young PwMS to adhere to their DMTs and healthy lifestyle choices, when they are in a developmental phase of high risk taking and

TABLE 5.1

Modifiable factors that may contribute to MS disease progression[30]

- Smoking
- Exercise
- Diet
- Sleep
- Comorbidities
- Infections
- Concomitant medications
- Drugs
- Social determinants of health
- Hormone replacement therapy
- Wellness

rebellion. Judgment, tact, and sensitivity are clearly indicated. Intellectual enrichment early in the disease course is recommended to support CR.[33]

The effects of recreational drugs on cognition in adolescents with MS are less well documented. We know that the onset of MS during childhood and adolescence negatively impacts brain growth and the normal maturation of neuronal networks. It is likely that the addition of cannabis could exacerbate CNS damage. In an American study, over one-half (64%) of young cannabis users with MS reported negative effects on their memory and focus.[34]

Key points – MS clinic management of cognition I: healthcare professional information and action

- There is some evidence that DMTs have a beneficial effect on cognition and it is likely that any agent slowing the progression of pathology will protect cognitive function.
- Cognitive impairment increases the risk of poor adherence to DMTs.
- PwMS' understanding of DMT risk management and monitoring may also be compromised, affecting adherence, and requiring extra support.
- Some rare but very serious side effects of the more effective DMTs, such as PML, may diminish cognition, and cognitive changes may be part of the presentation.
- A holistic approach to MS cognition management is required for optimal outcomes, including addressing DMTs, symptom management, increased risks, comorbidities, sleep, pain, and the general Brain Health approach.

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6 MS clinic management of cognition II: people with MS' engagement, information, and action

HEALTHCARE

In Chapter 5, we covered information and action for healthcare professionals (HCPs) managing people with multiple sclerosis (PwMS) with cognitive difficulties in the multiple sclerosis (MS) clinic. In this chapter, we cover best practice when engaging with PwMS to guide their education and actions. Both PwMS and HCPs recognize that successful engagement between them is crucial to achieving optimal health outcomes.[1] It has frequently been reported that HCPs consider physical symptoms, such as ambulation issues, imbalance, falls, and urinary incontinence, to be most important for the quality of life (QoL) of PwMS; however, PwMS consider non-physical symptoms, such as cognitive and memory problems, to be more significant.[2]

A qualitative study found that PwMS wished to be involved in decision-making around their care, but rarely found the information provided by HCPs to be helpful.[2] Instead, they searched the internet and visited various conversation platforms in social media, such as Facebook groups, for additional information.[3] For a HCP, a first step to successful engagement with a PwMS is to indicate that you share their concerns about cognitive impacts and that you will explain and discuss their experiences and management options in a way that is meaningful for them.

Communication

PwMS report a lack of open and empathic communication.[4] Figure 6.1 explores the broad context of health experience from several perspectives, and these must be considered in order to build rapport. To work successfully with PwMS with cognitive difficulties, HCPs need to amend their interaction style and adjust the content of their communication.

Interaction style. Complex information processing, such as understanding disease management advice, is heavily dependent on information processing speed (IPS), which is the most common and severe cognitive deficit in PwMS.[5] Slowing spoken delivery can help overcome this problem[6] and can be achieved easily in a relaxed manner, within normal speech parameters. This interaction style can also be shared with caregiver partners and modeled for them.

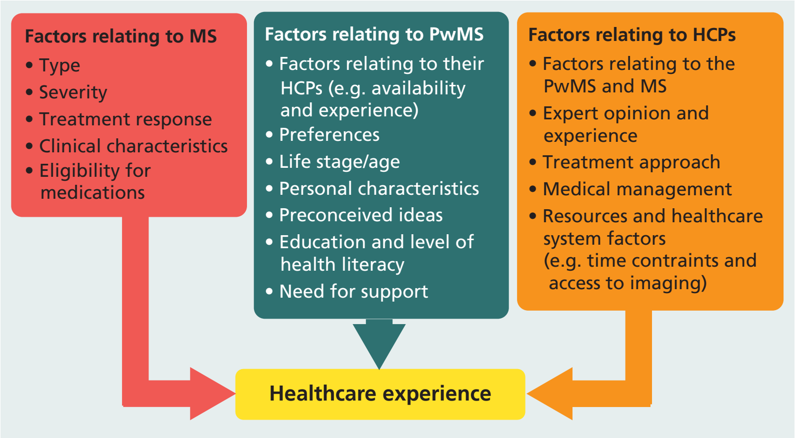

Figure 6.1 Model of the clinical context that influences healthcare experience, from a qualitative study that highlighted clear communication and self-management to be important for PwMS. Reproduced with permission under the terms of the Creative Commons Attribution 4.0 International (CC BY 4.0) license from Price et al., 2021.[4]

Content. To accommodate the slowed IPS of PwMS, HCPs should adjust the content of what they say, particularly when discussing important topics such as disease management and safety (Table 6.1). This can help avoid misunderstandings.[7]

Other aspects of communication that PwMS can find difficult are the so-called 'pragmatic' skills. They can find humor, sarcasm, and irony difficult to comprehend.[8] In a group of PwMS watching films of doctors and patients exchanging medical information, 17% made errors regarding figurative items and 32% made errors on humorous items, which was significantly worse than healthy controls.[9] They did much better on literal exchanges.

It appears that some PwMS have a primary deficit relating to humor, which relates to resolving incongruity. Others have difficulty appreciating humor secondary to a comprehension difficulty.[8] This may be because they are only taking in incomplete conversations due to slowed IPS and therefore the subtle nuances escape them.

TABLE 6.1

Strategies for successful communication with PwMS

- Use simple grammar and high-frequency words as much as possible
- Check the patient's understanding when giving important information
- Ask the PwMS to repeat and rehearse key points (this is known as 'self-generation' and is more effective than others repeating things to the PwMS)
- Avoid humor, sarcasm, and irony
- 'Play it straight' and use 'concrete' words (tangible words that refer to things that can be measured and observed)

Face masks. PwMS are particularly disadvantaged when those around them are wearing face masks. One study showed that people with relapsing remitting MS (RRMS) with an Expanded Disability Status Scale (EDSS) score of 4.0 or less (see Figure 3.1), who were less likely to have severe cognitive impairment, found it hard to recognize people wearing face masks (25% PwMS needed them to be removed to recognize faces compared with 4% of healthy controls).[10] Although it may not be safe to remove face masks in the clinic, all HCPs should be aware of the need to introduce themselves or other staff by name each time when meeting a PwMS while wearing a face mask.

In addition to difficulties recognizing people, a study of a group of patients with RRMS with no cognitive impairment detected using the Brief Repeatable Battery of Neuropsychological Tests (BRB-N) demonstrated that PwMS are less able to recognize facial expressions on the faces of masked individuals (from observing only the visible eye area and forehead).[11] Being mindful of this, HCPs wearing face masks should verbalize emotions to facilitate communication. Examples include:

- 'I'm pleased to hear that…'
- 'I have to say that worries me…'
- 'I'm sorry that you have had that experience…'

Treatment benefits and risks. Effective communication is particularly important when treatments and their related risks and benefits are discussed. One systematic review reported that disease-modifying treatment (DMT) risks and benefits are generally underestimated and overestimated by PwMS, respectively.[12] Treatments that could potentially offer substantial symptom improvement, delay in disease progression, or reduction in relapses are preferred, even when there is evidence of greater risk. Another review concluded that interventions to improve PwMS' understanding of treatment risks and benefits can be moderately successful.[13] The Benefit and Risk Information for Medication in Multiple Sclerosis (BRIMMS) protocol was empirically developed to present treatment risks and benefits to PwMS (Figure 6.2). When the BRIMMS protocol was used during consultation, PwMS retained more information and were more certain about their treatment choices than when following a 'usual' consultation. Cognitive status did not affect understanding or treatment certainty with the BRIMMS protocol, but was negatively linked in usual consultations.[14]

It is worth noting that many studies of PwMS have involved participants with early MS and very mild disability, and that communication challenges can be present for individuals with truly 'invisible' disability. It is a matter of courtesy and professionalism that we ensure we are engaging and communicating with PwMS optimally.

Information and action

Awareness. PwMS may not be aware that cognitive difficulties form part of the experience of MS for many people, and it is a good idea to introduce the possibility of them developing early on, partly so that the PwMS can take protective action with positive lifestyle choices. All of the MS charities in the UK have useful introductory materials that can be downloaded for free from their websites (see Useful resources, page 93). The Multiple Sclerosis Trust has a free, easily accessible, online cognition tool called 'StayingSmart' that explains how cognition can be affected in PwMS (mstrust.org.uk/a-z/stayingsmart). Some MS clinics organize 'cognition days' for patients based on StayingSmart. There are sections offering guidance on how to speak about cognitive problems with family, friends, and colleagues, and sections can be printed off to give to others. For PwMS who would like more detail and an opportunity to reflect, Jeffrey Gingold, a PwMS and MS advocate, has written a book about his experiences.[15]

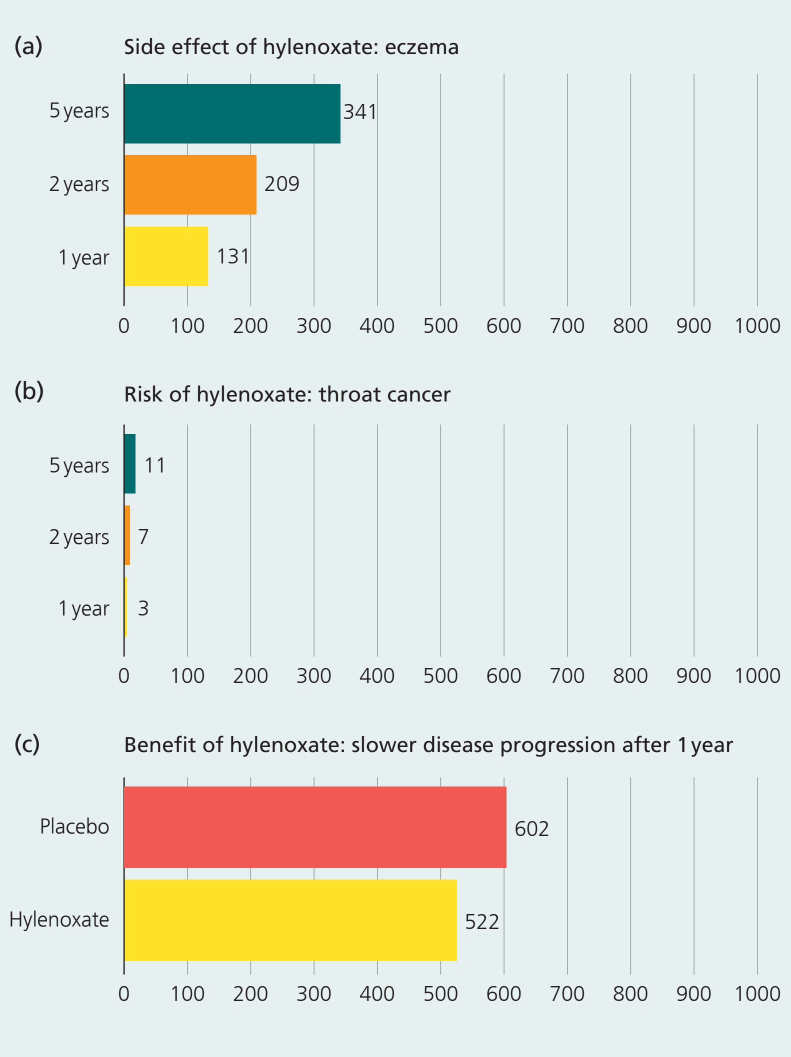

Figure 6.2 BRIMMS visual presentation of treatment side effects, risks and benefits for PwMS taking hylenoxate. Of 1000 PwMS taking hylenoxate (a) 131, 209 and 341 could develop eczema after 1, 2, and 5 years, respectively; (b) 3, 7 and 11 are at risk of developing throat cancer after 1, 2, and 5 years, respectively; (c) 522 will experience rapid disease progression (versus 602 PwMS taking placebo) after 1 year, so disease progression will slow for 80 PwMS taking the medication.[14]

Lifestyle choices. Obtaining information and advice has been reported to be a major stimulus for lifestyle change for PwMS,[16] as is feeling actively involved in one's own disease management. All of these motivators can be emphasized and facilitated by MS clinic staff. Motivational interviewing is a goal-driven counseling style that can help to engage individuals who are ambivalent about their ability either to adhere to a treatment regimen or to make, and sustain, beneficial lifestyle changes. If any staff have skills in motivational interviewing, they can be usefully employed to support lifestyle change, although the effect on maintaining change has not been established.[17]

As all professionals who work with PwMS know, components of disability and disadvantage tend to cluster and accrue in individuals. A study that looked at a large data set collected from the North American Research Committee on Multiple Sclerosis Registry reported that being a current smoker or having a moderate or severe level of disability, depression, fatigue, hand or bladder dysfunction, or minimal to mild spasticity were all associated with lower levels of physical activity.[18] It may be most helpful to begin by identifying one small change that can be successfully adopted, and then build on that.

Brain Health initiative. Once PwMS have been introduced to the possibility or reality of cognitive difficulties, most are pleased to learn about the Brain Health initiative, which enables them to do something constructive to protect their cognition by making informed lifestyle choices. Useful information and resources can be found at the MS Brain Health website (msbrainhealth.org). The National Health Service (NHS) website also has a useful section with advice on healthy lifestyle choices (nhs.uk/live-well). For patients who are engaged with the Brain Health initiative, the cognition agenda for PwMS (CAP) can be a useful way to support their actions (Figure 6.3).

Topic	Focus?	Action/goal	Resources needed	Support	Reward	Review
Exercise (example)	✓	*30-min walk, 3 times/week*	*Podcasts*	*Online support group*	*Pay-per-view film at end of week*	*In 1 month*
Disease-modifying treatment						
Other medications						
Exercise						
Eating						
Smoking						
Alcohol						
Self-prescribed medication						
Cognitive workout						
Sleep						

Figure 6.3 Example CAP form to help support PwMS improve brain health.

HCPs can help PwMS fill in a CAP form and decide on the program they want to follow, then contact them after 1 month or on an agreed review date to see how things are going. Example actions might include:

- exercising by walking three times per week, with the PwMS ensuring that they have podcasts to listen to and that they engage with an online support group
- smoking reduction, with the PwMS committing to limiting consumption to no more than 10 cigarettes per day, buying sufficient cigarettes for the week every weekend and reporting adherence at a weekly CAP group meeting
- cognitive workout by doing a daily newspaper crossword and discussing it with their caregiver partner for accountability.

Rewards should be individualized to the PwMS to ensure that they represent a sufficient incentive for action: for example, a pay-per-view film once per week, a specific purchase once per month, or a favorite food.

Physical activity. Most MS charities in the UK offer advice and guidance about exercise programs for PwMS, and many MS services have physical activity programs. A qualitative exploration of the feasibility and acceptability of one such program identified three key themes:

- ‘I can do this’: PwMS reported developing competence in physical activity, with confidence growing through goal setting and achievement
- ‘I felt valued’: the nurturing culture created a supportive, therapeutic relationship
- ‘What can I do?’: transition to intrinsic motivation for physical activity.[19]

These key drivers can be translated and applied to any lifestyle change, and can be used to structure discussion and support.

Sleep problems. Basic sleep hygiene advice and support may be enough to improve sleep problems if a PwMS is experiencing them. The NHS website has resources that PwMS can use by themselves (nhs.uk/every-mind-matters/mental-health-issues/sleep).

Risk monitoring. PwMS should be made aware that they need to pay attention to morbidity risks, and MS clinic staff need to regularly check in with PwMS about these issues and provide support as necessary. This applies to:

- disease management (including adherence and symptoms)
- work
- driving
- falls
- general wellbeing and participation.

Asking PwMS questions about work, driving, and falls is necessary during a consultation, because they may not volunteer the information or even be aware that early difficulties relate to MS. Issues are more likely to be managed successfully if addressed promptly and are likely to require specialist input (see Chapter 7), but the MS clinic physiotherapist may be able to assist if falls are occurring, and simple tips and tricks may support driving and employment. All of the UK MS charities have good resource materials addressing these issues, which can either be used by the PwMS alone or form the basis of in-clinic discussion and support.

General participation in social and lifestyle activities will reduce over the years for a minority of PwMS, and cognitive function is one predictor of this.[20] Monitoring of participation and encouraging regular social activities should also be part of a clinic visit.

Apart from the 'conventional' cognitive deficits, impairments in social cognition are probably involved in diminishing participation. Emotion perception difficulties have been linked to poorer social function in MS, independent of disability.[21]

Strategies to manage cognitive difficulties. Normalizing the experience of cognitive difficulties can be helpful for PwMS. Everyone experiences slips and errors, they may just happen more often for PwMS and can loom large in their minds. PwMS may remember and ruminate on such instances, while it is likely that the people around them did not pay them a lot of attention or cannot remember them.

Slowed information processing speed. When processing capacity is limited, it often helps to reduce the amount of information coming in. This may mean moving a desk to the corner of an open-plan office, or turning off the radio when having a conversation if an important topic is being discussed. When a number of cognitive tasks were tried with walking, the digit span backward task was shown to interfere most with gait speed and accuracy.[22] Increased complexity of the environment (narrow walkway, obstacles) affected both walking and cognition when PwMS were required to do both together, compared with healthy controls.[23]

Reduced IPS makes dual tasking harder, with any increase in task demand degrading the performance of both activities.[22,24] In the MS clinic setting, it makes sense to save difficult or complex conversations for when the PwMS is standing still or sitting, so that they can give the verbal input their full attention. It is also sensible to advise them not to listen to music while exercising or driving, and to use satellite navigation technology with caution.

Memory problems. A number of electronic solutions are available to help PwMS store information and provide reminders, ranging from mobile phones to more tailored devices. It is important to ensure that the PwMS can use the device effectively; evaluation and support may be required from specialists. Writing things down and using a diary or schedule assiduously may be alien to someone who has always been competent mentally and able to manage their daily tasks without conscious effort, but normalizing the behavior change by saying that lots of people keep a diary can be reassuring. Further useful strategies for PwMS are outlined in a book by Jeffrey Gingold and it may be worth referring patients to it.[25]

Engaging caregiver partners and colleagues

Caregiver partners are key allies for both PwMS and HCPs, and need support to play their important roles. Sharing information about cognitive impairment in MS can be very helpful. For example, consider a scenario where a working wife leaves her husband at home in the morning, because he has been forced to give up work due to MS, having asked that he do a load of laundry. Returning home tired in the evening, and finding that the laundry has not been done, it may be easy for her to conclude that her husband does not care, is lazy, or does not appreciate her enough to want to help with household chores. Knowing about cognitive issues in MS and that

PwMS may have difficulty remembering to do things may help to preserve the relationship and stop it souring.

It is no surprise that studies have consistently found that caregiver strain is increased if a PwMS has cognitive difficulties.[26] Cognitive and neuropsychiatric problems, reduced working memory, slowed IPS, executive dysfunction, and reduced verbal fluency have all been associated with increased burden and worse QoL of caregivers. A Cochrane review found telephone interventions for caregivers to be only slightly beneficial,[27] so it is important to have realistic expectations about how far a caregiver partner's wellbeing can be improved. Targeted work to evaluate specific interventions for caregivers of PwMS is ongoing.[28]

Most of the time, if you have the PwMS' consent, the more you can involve the caregiver partner the better. This means ensuring that they are fully informed about all treatment recommendations and symptom management advice. It is important to keep in mind that the MS clinic may be asking the caregiver to participate in care when they are already significantly burdened. The best way forward is usually to check with the PwMS regarding what they will accept help with and ask the caregiver what they feel they can contribute. If they have the time and other necessary resources, a caregiver can add an enormous amount to the cognitive care of a PwMS through:

- remembering and supporting the adoption of MS clinic advice
- supporting and encouraging participation in the CAP (see pages 65–7)
- monitoring cognitive function and picking up on decline and safety issues
- being alert to employment, driving, fall, and participation risks.

Caregiver reports of cognitive function of PwMS have been shown to align better with objective test scores than the perceptions of PwMS (see Chapter 4).

Colleagues can also be a great source of help. People who work with PwMS often want to help but do not understand the challenges that the PwMS is facing or what to do to support them. Encouraging the PwMS to talk to colleagues and possibly even share resources could facilitate good outcomes. Some multidisciplinary teams offer an employment support service, including workplace visits.

Pediatric patients. There is less evidence to guide MS clinic interventions for children and young PwMS than for adults. DMTs are the cornerstone of management, although guidance on strategies to optimize wellbeing states that high-level vitamin D intake and a diet low in saturated fat are associated with lower relapse rates.[29] Regular exercise can improve fatigue and sleep problems, and behavioral strategies for mood regulation and sleep hygiene can be helpful. Any issues regarding school and social functioning need to be carefully monitored and managed by the MS clinic.[29] Although the etiology of pediatric MS remains unclear, investigation of whether primary prevention of pediatric MS is feasible has begun and may identify children at increased risk of developing MS who would benefit from screening.[30]

Key points – MS clinic management of cognition II: people with MS’ engagement, information, and action

- HCP interaction styles should be modified to accommodate PwMS with cognitive impairment.
- Accurate and accessible information is especially important in relation to DMTs and other disease management priorities.
- StayingSmart is a free online cognition tool designed for PwMS.
- PwMS should be encouraged to actively manage their cognition, including engaging with the Brain Health initiative.
- The CAP is a useful guide and prompt for PwMS’ self-management of cognition.
- Caregiver partners are key allies for both PwMS and HCPs, and need support to play their important roles.

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7 Additional specialist input

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Not all multiple sclerosis (MS) clinics will have access to specialist support for cognition,[1] and services or professionals badged as 'specialist' may not always have specific expertise or experience related to MS cognition.[2] In such circumstances, a certain amount of negotiation and collaboration will be required to ensure a successful outcome.

Specialist cognitive assessment

If a person with MS (PwMS) or their caregiver partner is reporting persistent and troubling difficulties, which you feel confident have a cognitive basis because you have established cognitive impairment through in-clinic testing, it is worth seeking an external specialist cognitive assessment, if that is an option for your clinical setting. If the external specialist professional or service frequently provides input to your MS clinic, it may be possible to develop a standard referral and report template that is helpful to all parties (Table 7.1). The referral letter should be shared with the PwMS and their caregiver whenever possible or, even better, written collaboratively with them. It is a good idea to prepare the PwMS for specialist cognitive assessment, so they know what to expect. StayingSmart (mstrust.org.uk/resources/staying-smart) and many National Health Service (NHS) Trusts have online introductions to how cognitive assessments are done.

If ongoing support from a cognitive specialist is not possible, a joint (online) conference for all stakeholders can be helpful for two reasons:

- the PwMS and clinic staff can ask questions
- it signals the importance of cognition management to the PwMS and the MS clinic's commitment to it.

Sending a short summary to the PwMS and their caregiver partner after the conference can be very helpful. It is worth noting that a cognitive assessment and feedback alone have been linked to improvements in perceived everyday cognitive functioning, self-efficacy, and even the mood of PwMS.[3]

It is worth being cautious if the only specialist neuropsychology assessment service that you can access is a dementia service, often called a 'memory clinic'. In such circumstances, extra care and discussion may be necessary with the PwMS concerning their illness and how their cognitive experience does, and will continue to, differ

TABLE 7.1

Suggested content for a specialist cognitive assessment referral and report form

Reason for referral

- Concrete descriptions and frequency of events, reported by the PwMS/caregiver partner/MS clinic staff/PwMS' work colleagues/social services/primary care provider
- History of previous cognitive problems

Brief personal summary

- Age, marital status, family, education, work history
- PwMS' perception of problem(s)
- Family/caregiver partner involvement and their perception of problem(s)
- Important/recent life events

Brief disease summary

- MS duration, phenotype, medications, disability/ambulatory status (in words, not just EDSS score), current challenges linked to MS
- Comorbidities (physical and psychiatric), current treatment

Previous and current cognitive test results

- Scores and summaries of results

Previous specialist cognitive input and outcomes

- Descriptions, frequency, and outcomes

Requested response

- Cognitive profiling
- Management advice
- Recommended resources: information (print/online), training/ rehabilitation program
- Summary for PwMS and caregiver partner
- Summary for PwMS' work colleagues
- Ongoing input
- Other recommended specialist service(s)

EDSS, Expanded Disability Status Scale.

from general dementia. MS usually has a circumscribed effect on cognition (information processing speed [IPS] and memory) and is typically mild and slow to progress (see Chapters 2 and 3). In contrast, dementia (for example, Alzheimer disease) is usually accompanied by broader-range and faster cognitive decline.[4]

Cognitive rehabilitation

Cognitive rehabilitation includes a variety of behavioral treatments that improve cognitive functions and activities of daily living.[5] To date, promising results have mainly come from studies involving patients with relapsing remitting MS (RRMS);[6] however, there is some evidence that it is helpful for people with advanced MS (for example, in one study of 18 patients with a median Expanded Disability Status Scale [EDSS] score of 7.5).[6–8]

Restorative cognitive rehabilitation is designed to reinforce, strengthen, and reinstate cognitive skills, usually by using repetitive computer programs. IPS and attention deficits are most often treated by restorative computer programs, which offer repetitive and rapid presentation of stimuli.[8] RehaCom (hasomed.de/en/products/rehacom) is one of the most commonly used programs in research, and PwMS have been shown to be adherent to a home-delivered RehaCom program, which improved IPS.[9] Dual-task training programs have been reported to improve executive functions.[10]

Compensatory cognitive rehabilitation helps PwMS offset cognitive difficulties by using internal (for example, visualization) and external (for example, diaries) strategies.[5] There is most research backing for the Kessler Foundation Modified Story Memory Technique.[11,12] This utilizes contextualization (such as developing a story that incorporates items to be remembered) and visual imagery (such as visualizing items to be remembered) to support new learning and memory for cognitively impaired PwMS. This approach involves fairly lengthy group interventions over several weeks and is therefore resource heavy.[11]

Studies published to date provide clear descriptions of interventions (for example, restorative approaches, compensatory strategies, or environmental modifications) and practical details (such as targeted cognitive domain, treatment frequency, and duration). The original classical studies of cognitive rehabilitation have reported interventions relying on sequential clinic attendance. Because of resource implications, there is now increasing interest in the comparative efficacy of clinic versus home-based interventions and group versus individual delivery,[13] although the relative merits of individual and group rehabilitation remain unresolved. Increasingly, hybrid designs with some clinic attendances supported by home-based work have shown promise. The MAPSS-MS (Memory, Attention, Problem Solving Skills in MS) program, for example, requires eight weekly 2-hour group sessions, with three additional 45-minute computer sessions each week.[14] Such approaches remain resource heavy, however, but it is possible that digital health technology may improve the feasibility of these interventions for mass roll out.[13]

Driving

In the UK, driving assessments can be arranged via Driving Mobility (drivingmobility.org.uk). This charity can also offer advice on how MS may impact a person's ability to make appropriate decisions with regards to safe driving, address disability profiles that require special modifications to a motor vehicle for safety, and advise on wheelchair-accessible vehicles.

Employment

Finding work. The UK government provides statutory support services to help people with disability maintain or find new employment (gov.uk/looking-for-work-if-disabled). Job centers have work coaches who can advise PwMS about local employment opportunities and financial support options. PwMS have been shown to benefit less from standard vocational rehabilitation than people with other medical conditions, and this has been attributed to a failure to address cognitive issues, particularly if the PwMS is already unemployed.[15] According to PwMS, individualized support that is offered early is most effective.[16]

Working with employers. Supporting PwMS in the workplace tends to require significant resources.[17] The charity MS-UK (ms-uk.org) engages with employers to help them understand the challenges MS poses in the work environment, while the MS Society (mssociety.org.uk) provides legal advice regarding employment to PwMS. Some MS clinics (for example, the National Hospital for Neurology and Neurosurgery in London) have developed particular skills in MS employment support.[18]

Sleep

There is promising evidence that specialist input to treat sleep problems in PwMS can be effective; however, it is worth noting that PwMS with higher levels of anxiety, fatigue, and depression report lower-quality sleep, and it is probably worth reviewing these symptoms before seeking a specialist referral for sleep management.[19] Cognitive behavioral therapy has been shown to improve sleep for PwMS,[20] and the development of telehealth programs has improved accessibility.[21] The Sleep Apnoea Trust (sleep-apnoea-trust.org) provides a list of sleep clinics in the UK, and sleep clinic staff may be willing to consult or mentor staff in MS clinics.

Pediatric multiple sclerosis

Restorative cognitive rehabilitation may work in pediatric MS[22] although evidence is sparse.[23]

Key points – additional specialist input

- If an external specialist cognitive assessment is an option for your clinical setting, it may be worth discussing with the specialist neuropsychology service what information is most useful to include in a referral and subsequent report, and developing a standard template that is helpful to all parties.
- There is good evidence that cognitive rehabilitation can improve the cognitive function of PwMS, but implementation of validated protocols requires extensive resources.
- Standard vocational rehabilitation is less effective for PwMS than for people with other medical conditions; this is believed to be because it does not address cognitive issues.
- Specialist input to treat sleep problems in PwMS can be effective, but it is worth reviewing a PwMS' anxiety, fatigue, and depression levels, and taking appropriate action, if necessary, before seeking referral.

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8 Difficult conversations

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Best practice

Talking about cognition can be difficult because awareness and understanding may differ between key people, and staff in multiple sclerosis (MS) clinics may not have experience of, or have developed expertise in, discussing cognition. In general, an empathic matter-of-fact approach, including concrete words and direct experiences, works best. The 'SPIKES' model, although developed for use in oncology, has been shown to improve communication in a variety of medical settings (Table 8.1).[1] It is designed to fulfill the following objectives:

- disclosing difficult news
- gathering information from the patient
- transmitting new information
- providing support to the patient
- eliciting the patient's collaboration in developing a strategy or treatment plan for the future.

The SPIKES approach can be used as a flexible guideline for structuring communication. You should also regularly check in with the person with MS (PwMS) and/or their caregiver partner that they are comfortable with the conversation and are happy for it to proceed, and ensure that they are given ample opportunity to ask questions. Careful checking that the PwMS or caregiver partner has an understanding of 'cognition' and other terms used, the usual pattern of cognitive difficulties in MS (mild and restricted, slow to progress), and how this differs from other situations such as normal aging and dementia are all important. 'Concrete' explanations and examples are valuable and preferred: for example, 'slowed information processing speed (IPS) can be likened to reduced bandwidth or slowing of the internal internet'. Healthcare professionals (HCPs) should expect to repeat information within and across consultations, need to check understanding and remembering, and always encourage management and protection (for example, the Brain Health initiative).

TABLE 8.1

Summary of the SPIKES approach

Setting

- Arrange for some privacy
- Involve caregiver partner
- Sit down: be at the same level as the PwMS, especially if they are in a wheelchair
- Make connection with the PwMS (eye contact)
- Manage time constraints and interruptions

Perception

- Use open-ended questions to understand how the PwMS perceives their situation and the context of cognition in MS

Invitation

- Check the PwMS is ready to talk about cognition; pick up on previous conversations or difficulties that may be linked to cognition

Knowledge

- Start at the level of comprehension and vocabulary of the PwMS, and be concrete

Empathy/emotions

- Imagine how you would wish to have this matter discussed as a PwMS; acknowledge any emotions and check feelings/reactions

Strategy and summary

- Summarize what has been discussed and set out a plan of action

Common scenarios and how to approach them

Scenario 1: broaching the subject of cognitive difficulties at diagnosis. There is evidence that PwMS would like to be told about cognitive involvement from the start.[2]

Knowledge. Begin the conversation by finding out what the PwMS already knows. Speak about cognitive impairments colloquially: for example, ‘difficulties with memory and concentration’, and discuss the usual MS cognitive profile. Explain that cognitive impairment is a separate process from mood and fatigue, although low mood or fatigue can make a person feel that cognition is diminished. Ensure that the PwMS understands that this is different from normal aging, and can in some ways be thought of as accelerated aging, and that they understand how the MS cognitive profile differs from that of dementia:

- mild
- circumscribed
- develops slowly
- can be unchanged for many years.

Explain that many PwMS lead full, productive lives with only mild cognitive difficulties and introduce the PwMS to the Brain Health initiative (msbrainhealth.org). Also explain that time matters in MS and that support will be available should they experience cognitive difficulties. This is the rationale for annual cognitive testing. Signpost to resources and further information if the PwMS would like them.

Scenario 2: a caregiver contacts you about a patient’s cognitive difficulties. Begin by explaining that you can listen but cannot disclose any information about the PwMS, unless you have previously been given permission by the PwMS to share information with the caregiver. Listen actively and sympathetically, and indicate that you understand and are paying close attention (especially important on the phone) to form a clear picture of the situation the caregiver is communicating to you.

Cover the topics set out in the ‘Knowledge’ section of scenario 1 before finding out what the PwMS has shared with the caregiver with regard to what they know and how they perceive their cognitive function. If there are no safeguarding issues or criminal implications, try to persuade the caregiver to attend a clinic appointment with the PwMS, so that the issue can be raised naturally in that setting. MS clinic staff in the consultation can raise the issue as a matter-of-fact enquiry.

During the consultation. Use the 'Knowledge' section of scenario 1 to structure a conversation with both the caregiver and PwMS. Emphasize that cognitive difficulties are a typical part of MS (if appropriate) and any forgetfulness does not reflect how much the PwMS cares about the caregiver or their home life.

If there are any safeguarding issues or criminal implications, take advice from your manager and follow National Health Service (NHS) Trust policy and professional guidelines.

Scenario 3: preparing a PwMS for a clinic cognitive assessment. Begin by checking that the MS clinic has triaged for fatigue and mood and addressed them adequately, if appropriate. If not, arrange for a fatigue and depression assessment. Use the 'Knowledge' section of scenario 1 to introduce the subject of cognitive difficulties in MS. Explain who the information gathered from a clinic cognitive assessment will be shared with and that the PwMS has control over this, up to a point (legal position). Note that they may have concerns about their employer, driving authorities, or custody hearings accessing this information.

Once this has been done, explain that the tests involved in the assessment are specifically designed to pick up the difficulties that PwMS are most likely to experience and that they have been carefully researched and are in use all over the world. Also explain that the clinic cognitive assessment will be able to pick up even small changes in memory and concentration, and any detected will be extra motivation for the PwMS to adopt or work harder at the Brain Health initiative (msbrainhealth.org). In addition, the results of the assessment will enable the MS clinic staff to communicate more effectively with the PwMS and amend their clinic services to accommodate these difficulties.

Having set the scene, explain to the PwMS what will happen during the tests, so they know what to expect, and that feedback will be available 1 or 2 weeks after testing. You can also signpost to resources and further information if the PwMS would like them (see Useful resources for suggestions).

Scenario 4: providing feedback to a PwMS about their cognitive assessment. PwMS have differing preferences regarding who should give cognitive assessment results; some prefer a neurologist, especially if cognitive decline has been demonstrated, so that they can ask questions, while others prefer a nurse with whom they have established a relationship and who can offer longer appointments.[3]

When relaying the results of a cognitive assessment, you should aim for a semi-structured, interactive, collaborative, and empathic discussion.[4] Be concrete and matter of fact, and link results with everyday examples, relating the findings of the assessment to the experience and report of the PwMS and their caregiver partner. Your comments need to connect with the specific life context and difficulties that they are encountering. Give a balanced view, including mention of cognitive skills that are demonstrably intact or generally unaffected by MS.

In a randomized controlled trial comparing cognitive assessment with feedback with no assessment and no feedback, the assessment with feedback group reported fewer problems with everyday cognitive functioning, increased self-efficacy for managing MS, and decreased stress and depression 1 month after the feedback was received.[4] The feedback was delivered in a face-to-face setting, adopting a semi-structured, interactive, collaborative, and empathic style. Where appropriate, feedback was structured according to the SPIKES approach (see Table 8.1). The content of the advice was tailored to the needs of individual participants.

Begin your conversation with the PwMS by finding out what they already know. Follow the guidance outlined in scenarios 1 and 3 above.

If objective findings demonstrate less cognitive impairment than the PwMS' self-perceived cognitive status, explain that people tend to remember particularly embarrassing or public difficulties, and that the tests make a broad comparison with the general population.

If cognitive impairment is demonstrated, advise that a clinic cognitive assessment can pick up even small changes in memory and concentration. Provide details about whether the assessment indicates that IPS is slowed and/or verbal and/or visual memory are affected. Give examples of what this might mean in everyday life and suggest management strategies.

If the caregiver partner was not present at the assessment or related consultations, including this one, request permission from the PwMS to share the results with them, or better yet, set up an appointment with both the PwMS and the caregiver partner to discuss the results. Explain the value of this and the importance of caregiver support to the PwMS.

Scenario 5: legal process related to cognition. A PwMS or caregiver partner may seek your advice about power of attorney or making a will. These issues are best dealt with under the direction of a solicitor, who may commission reports from the multidisciplinary team. Further information can be found on the UK Government's website (gov.uk/power-of-attorney). PwMS with mild cognitive deficits typically remain able to make legally valid decisions about wills, but this validity needs to be established first. In the UK, Citizens Advice may be able to help PwMS and their caregiver partners access free legal advice (citizensadvice.org.uk).

Key points – difficult conversations

- Talking about cognition can be difficult because awareness and understanding may differ between key people.
- The SPIKES approach (setting, perception, invitation, knowledge, empathy/emotions, and strategy and summary) is useful for structuring difficult conversations.
- Sharing information about a PwMS' cognitive profile is best done in a concrete, matter-of-fact way, linking the findings with everyday activities.
- 'Concrete' explanations and examples are valuable and preferred, such as 'slowed IPS can be likened to reduced bandwidth, or slowing of the internal internet'.
- For legal process relating to cognition, such as power of attorney or making a will, refer the matter to a solicitor.

References

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Useful resources

UK

Citizens Advice
citizensadvice.org.uk

Driving Mobility
drivingmobility.org.uk/assessments/driving-assessments

Memory Aids and Tools
alzheimers.org.uk/get-support/staying-independent/memory-aids-and-tools

MS Brain Health
For professionals: msbrainhealth.org

For people with MS: msbrainhealth.org/people-with-ms

MS Society
mssociety.org.uk

Legal advice regarding employment for people with MS: mssociety.org.uk/care-and-support/financial-help/legal-advice

MS-UK
ms-uk.org

Multiple Sclerosis Trust
mstrust.org.uk

StayingSmart, an online resource for people who want to know, or know more, about how MS can affect thinking: mstrust.org.uk/a-z/stayingsmart

StayingSmart also has a useful summary of how a cognitive assessment is conducted: mstrust.org.uk/information-support/staying-smart

The Multiple Sclerosis Trust provides a current summary of disease-modifying treatment information for people with MS: mstrust.org.uk/information-support/ms-drugs-treatments/disease-modifying-drugs-dmds

National Health Service
Advice on healthy living, including eating a balanced diet, healthy weight, exercise, quitting smoking and drinking less alcohol: nhs.uk/live-well

Advice on the importance and improvement of sleep: nhs.uk/every-mind-matters/mental-health-issues/sleep

National Institute for Health and Care Excellence
Multiple sclerosis in adults: management. NICE guideline [NG220.] 2022: nice.org.uk/guidance/ng220

Guidelines relating to products: nice.org.uk/guidance/conditions-and-diseases/neurological-conditions/multiple-sclerosis/products

RehaCom
hasomed.de/en/products/rehacom

Sleep Apnoea Trust
List of sleep clinics in the UK: sleep-apnoea-trust.org/sleep-apnoea-trust-list-nhs-sleep-clinics-uk

UK Government
Information about support available to help people with disability find employment: gov.uk/looking-for-work-if-disabled

Information about power of attorney: gov.uk/power-of-attorney

People with MS' experience of cognition
The following texts can enhance healthcare professionals' understanding and reflection, and be useful for working with people with MS and caregiver partners.

Gingold JN. *Facing the Cognitive Challenges of Multiple Sclerosis*, 2nd edn. Demos Medical Publishing, 2011.

Gingold JN. *Mental Sharpening Stones: Manage the Cognitive Challenges of Multiple Sclerosis*. Demos Medical Publishing, 2008.

Further reading

Writing a clinic handbook, we have not been able to include lengthy case studies or detailed reviews of the literature. Readers seeking this level of content are referred to Anthony Feinstein's *Mind, Mood, and Memory. The Neurobehavioral Consequences of Multiple Sclerosis* (Johns Hopkins University Press, 2022), which also covers behavioral change and neuropsychiatric impacts. The case studies could also be used judiciously with some people with MS and their caregiver partners. For the specialist reader, there is also *Cognition and Behavior in Multiple Sclerosis* edited by John DeLuca and Brian M Sandroff (American Psychological Association, 2018).

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