Cognitive Function in Multiple Sclerosis – A Roundtable Discussion

Working Party

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In June 2007, a panel of healthcare professionals with a strong interest in and/or practical experience of cognitive problems in people with multiple sclerosis (MS) met to explore the potential for routine screening of cognitive function in the clinical management of people with MS. The purpose would be to examine whether changes in cognitive function were significantly affecting a person's life. This paper provides a summary report of the group's discussion and views on cognitive function and screening, including the measures being used, their appropriateness for use in MS clinical services and the potential for a measure that encourages healthcare professionals to monitor cognitive function routinely.

Cognitive dysfunction affects up to 65% of people with MS.[1] It threatens confidence and self-esteem and can disrupt employment, social interactions, and daily routines.[2,3] Symptoms of cognitive dysfunction, which can cause significant upset for patients and families, are subtle and complex and therefore, can be challenging to identify. They may produce memory decline which affects 40-60% of individuals,[4] reduction in: new learning capacity,[1] verbal working memory,[5] visual memory and auditory memory.[6] Other changes include dysexecutive symptoms, with a reduced ability to engage in testing,[7] attention deficits,[8] reduction in processing speed[9] and intellectual decline.[10] There was a view during the discussion that many people with MS are unaware of the meaning of cognitive changes and may confuse them with symptoms of mental health problems.

Rehabilitation and cognitive decline

Rehabilitation can be regarded as a problem solving and educational process aimed at reducing the level of disability and increasing the level of independence. However, this is always within the limitations imposed both by available resources and by the underlying disease process.[11] It encompasses the ability to learn new information and adapt to new ways of functioning, which utilises feedback, taking into account cognitive ability. Therefore, cognitive and related impairments are likely to have an impact on rehabilitation when domains of cognition such as communication, recall, processing speed, problems in abstract thinking, coping strategies, mood and relationships are affected.

Table A: Reasons for cognitive screening

- *To provide a baseline as a measure of deterioration*
- *To give reassurance*
- *To inform how a multidisciplinary team should work with a patient.*
- *To inform on intervention/medical treatment*
- *Cognitive Rehabilitation*
  - *Individual*
  - *Groups*
  - *Carer Support/education*
- *Research*
- *Highlighting to commissioners the need for resources and coherent psychological services to address the various problems arising as a result of cognitive impairment.*

healthcare providers should offer periodic screening and/or assessment of cognitive function

According to a recent observation of one of the group members, approximately 90% of people with MS who were admitted to a rehabilitation centre agree with the following statements to some degree: 'I begin to talk and forget what I was going to say' and 'I have difficulty finding words when trying to explain things'.[11] However, when the same patients were asked if they had speech problems, there was a lack of awareness of such problems, suggesting that cognitive impairment may limit the strategies which can be adopted to cope with illness, such as problem solving (if working memory is impaired) and organisation, if there are dysexecutive problems. Given that people with MS deteriorate, learning to cope and adjust is an important part of maintaining a person's quality of life. From the group's experience it was felt that people generally cope better if they feel they have control over what happens to them and a choice in their lifestyle.[11]

Mood changes are common in people with MS, with up to 42% reported to suffer significant depression.[12] Depression itself can affect short term memory, learning and attention[12] and anxiety may also impair attention[14] but the relationship between cognition and mood is complex. One viewpoint at the meeting was that a person's lack of expression of distress could be due to communication or cognitive problems.

The group generally felt that there is a relation between fatigue and cognitive problems and that recognising these links, treating the fatigue and/or associated depression, may reduce the impact of cognitive decline on daily life.[15] Developing and using strategies for dealing with cognitive problems, such as memory impairment, may also help improve general well-being.

Cognitive impairment may put a strain on the carer/patient relationship. For example forgetting,

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repeating one-self and confusion can lead to the need to work with patients and their carers on ways to manage the cognitive problems together. Executive problems may also affect behaviour, leading to difficulties in relationships with staff and others.

Monitoring cognitive function in clinical practice

The experience of practicing Clinical Neuropsychology within a Neuro-rehabilitation Service highlighted several practical reasons why assessment of cognitive function is not routinely performed, including the fact that tests are long and not standardised for people with MS, the limited availability of assessments for people with physical difficulties, including poor vision, communication problems and fatigue, and lack of resources. The rationale for cognitive assessment needs to be established and consideration needs to be given to when, where, why and how to carry out cognitive assessment as well by whom. One view was that it is important to take into consideration that screening someone has the potential to unnecessarily highlight a cognitive problem.

It has been recommended that healthcare providers should offer periodic screening and/or assessment of cognitive function,[16] as deficits may not always be reported or noticed. For example, The NICE guidelines state: 'Any person with MS complaining of cognitive problems… should be offered a formal cognitive assessment' and yet it is an area that is not assessed routinely.[17] Early screening would be helpful and it may be useful to ask questions both to elicit information and also to give reassurance. Patients are often relieved to be told that cognitive changes they may be experiencing, are not dementia and that they are not 'going mad'.

At the meeting, several reasons why screening for changes in cognitive function may be helpful were raised (Table A). Although consultation rates have been found to increase as cognitive function worsens, the generally held view was that once an appropriate care package is put in place the rate of consultation lessens thereafter. It is feasible that early recognition and intervention in cognitive dysfunction can have a positive impact, because people are likely to be able to stay in work for longer and maintain relationships for longer. Early recognition of cognitive function decline enables early intervention. Once memory loss becomes too impaired, teaching strategies to cope become of little use.

The most appropriate format for cognitive assessment remains unclear. Asking specific questions about problems at work, in daily life and hobbies may be beneficial. However, asking global questions such as "Are you having memory problems?" can be inappropriate as they may lead to false positives and conflicting information. Subtle enquiry with a patient or carer may educate patients and carers, highlight concerns and reduce anxiety. Although the necessity to perform in-depth assessments at the point of diagnosis remains debatable, performing in-depth neuropsychological assessments soon after a diagnosis of MS may sometimes be helpful especially when employment is threatened, there are difficulties with independence in the home or education problems.

Routine screening for cognitive dysfunction in MS

To encourage cognitive screening of people diagnosed with MS, the measure should ideally be brief, sensitive, and specific, with a clear cut-off point (i.e. provide a score to indicate that further evaluation is required) and be independently validated. It should also be able to evaluate specific cognitive domains including; memory, attention, executive abilities and speed of processing. It should be independent of mood, fatigue and disability. It is clear that there is a drive for something brief and which does not necessarily require the involvement of a neuropsychologist, although it is important not to overemphasise the need to save time. Detailed assessment of cognitive function requires the appropriate time. It is difficult to know from the outset which cognitive functions are impaired and consequently measures of most cognitive domains should be included.

Two main strategies have been used to assess cognitive function in people with MS. These are self-report measures e.g. MSNQ (MS Neuropsychological Questionnaire),[18] and short batteries of cognitive tests.

Discussion focussed on the MSNQ, which had general appeal because it is short and easy to administer. There are only 15 questions rated on a 5 point scale. It is non-invasive, standardised and validated.[18] However, with the self report form of the MSNQ, a replication study found the specificity to be only 0.6, with false negatives seen in people with low mood.[19] The self report version was highly correlated with mood and not significantly correlated with cognitive tests.[19] The informant MSNQ shows higher sensitivity and speci-

Table B: Neuropsychological Tests included in the MACFIMS

Test	*Domain*
Benton Judgement of Line Orientation Test	*Visual/Spatial Perception*
Controlled Oral Word Association Test	*Generative Verbal Fluency*
California Verbal Learning Test, Second Edition	*Auditory/Verbal Learning and Memory*
Brief Visuospatial Memory Test – Revised	*Visual/Spatial Learning and Memory*
Paced Auditory Serial Addition Test	*Processing Speed and Working Memory*
Symbol Digit Modalities Test	*Processing Speed and Working Memory*
Delis Kaplan Executive Function System	*Executive Function*

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Identification of cognitive deficits in people with MS requires greater emphasis

ficity than the self report version[19] and is significantly correlated with cognitive tests and not with mood. Self report and informant measures can lead to conflicting results, but each provides useful information.

Cognitive tests have the advantage of standardisation and are usually independent of mood. The Addenbrookes Cognitive Examination – Revised (ACE-R), is used in clinical practice to monitor cognitive function and takes between 10 minutes to half an hour. Although the ACE-R has not been validated for use with MS patients it had been used by a member of the group. It is not sensitive to mild cognitive decline. There are timed elements within the assessment, which is an advantage, as slowness is a common problem in MS patients.[13] The ACE-R includes a drawing which the group felt may limit the completion of the assessment, although it is unlikely to misclassify patients on the basis of one item.

Undue length is a concern with some cognitive test batteries, a disadvantage in fatigued patients especially. They take from 20 minutes, for example for the MMSE, up to 90 minutes for the MACFIMS (Minimum Assessment of Cognitive Function in MS), because they assess a number of different domains (Table B).[19] Furthermore, some tests require motor skills that limit their applicability to severely physically disabled patients. Other drawbacks include poor specificity and sensitivity; and the batteries are not always relevant to the usual pattern of cognitive impairment in people with MS,

There have been attempts to compare the effectiveness of the tests. Aupperle et al[20] found that the sensitivity of the Neuropsychological Screening Battery for Multiple Sclerosis (NPSBMS) and the Screening Examination for Cognitive Impairment (SEFCI) was greater than the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). The best sensitivity was achieved from a combination of the NPSBMS and Symbol Digit Modalities Test (SDMT). They suggested that if one test is to be used the Symbol Digit Modalities Test (SDMT) may be the most sensitive.

Conclusion and summary

The identification of cognitive deficits in people with MS requires greater emphasis. However, to introduce cognitive assessment into routine clinical management is challenging. One approach may be to develop a simple measure that incorporates questions pertaining to cognitive function while at the same time going over the main challenges that a person with MS has to cope with. If at this initial screen a decline in cognitive function is identified, then further cognitive screening (e.g the MSNQ) could be implemented. The development of a measure would help to raise awareness of cognitive problems and would guide professionals when attempting to determine overall priorities for the patient, carer and healthcare professionals. It should therefore, be designed to monitor the patient's, carer's and healthcare professional's perspectives.

Enabling patients, professionals and carers to contribute equally to the assessment of cognitive function may help to provide a more balanced perspective. This balanced approach could encourage a discussion of areas where the patient and carer would wish to concentrate, but also it could help the healthcare professionals to identify other areas of concern. It is therefore vital that any screening or assessment should be patient led and done within the context of a professional relationship.

References

1. Rao SM, Leo GJ, Ellington L, Nauertz T, Bernardin L, Unveragt F. *Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns and prediction.* Neurology. 1991;41:685-91.
2. Amato MP, Ponziani G, Pracucci G, Bracco L, Siracusa G, Amaducci L. *Cognitive impairment in early-onset multiple sclerosis: pattern, predictors, and impact on everyday life in a 4-year follow-up.* Arch Neurol 1995;52:168-72.
3. Rao SM, Leo GJ, Ellington L, Nauertz T, Bernardin L, Unveragt F. *Cognitive dysfunction in multiple sclerosis. II. Impact on employment and social functioning.* Neurology. 1991;41:692-6.
4. Grafman J, Rao S, Litvan I. *Disorder of memory. In Rao SM (ed) Neurobehavioral aspects of multiple sclerosis.* Oxford., New York, 1990;pp102-17.
5. Rao SM, Grafman J, DiGiulio D et al. *Memory dysfunction in multiple sclerosis: its relation to working memory, semantic encoding and implicit learning.* Neuropsychology 1993;7:364-74.
6. Brassington, JC, and Marsh, NV. *Neuropsychological aspects of multiple sclerosis.* Neuropsychology Review. 1998;8:43-77.
7. Rao SM. *Neuropsychology of multiple sclerosis: a critical review.* J Clin Exp Neuropsychol 1986;8:503-42.
8. Beatty WW and Monson N. *Picture and motor sequencing in multiple sclerosis.* J Clin Exp Neuropsychol 1994;16:165-72.
9. Diamond BJ, DeLuca J, Kim H, Kelley SM. *The question of disproportionate impairments in visual and auditory information processing in multiple sclerosis.* J Clin Exp Neuropsychol 1997;19:34-42.
10 Ron MA, Callanan MM, Warrington EK. *Cognitive abnormalities in multiple sclerosis: a psychometric and MRI study.* Psychol Med. 1991;21(1):59-68.
11. White M. Paper in preparation.
12. Jefferies K. *The neuropsychiatry of multiple sclerosis.* Advances in Psychiatric Treatment 2006;12:214-20.
13. Winkelmann A, Engel C, Apel A, Zettl UK. *Cognitive Impairment in multiple sclerosis.* J Neurol 2007:254(suppl 2):35-42.
14. Maurelli M, Marchioni E, Cerretano R, Bosone D, Bergamaschi R, Citterio A, et al. *Neuropsychological assessment in MS: clinical neurophysiological and neuroradiological relationships.* Acta Neurol Scand 1992;86:124-8.
15. Parmenter BA, Denney DR, lynch SG. *The cognitive performance of patients with multiple sclerosis during periods of high and low fatigue.* Mult. Scler. 2003;9:111-8.
16. Medical Advisory Board of the National Multiple Sclerosis Society (NMSS). *Assessment and Management of Cognitive Impairment in Multiple Sclerosis 2006,* US Neurological Disease.
17. National Institute for Health and Clinical Excellence (NICE). *Management of multiple sclerosis in primary and secondary care.* 2003.
18 Benedict RHB, Munshauer FE, Linn R, Miller C, Foley FW, Jacobs LD. *Screening for multiple sclerosis cognitive impairment using a self-adminstered 15-item questionnaire.* Mult Scler. 2003;9:95-101.
19. Benedict RHB. *Integrating Cognitive Function Screening and Assessment into Routine Care of Multiple Sclerosis Patients.* CNS Spectrums. 2005;10(5):384-91.
20. Aupperle RL, Beatty WW, Shelton F de NAP and Gontkovsky ST. *Three screening batteries to detect cognitive impairment in multiple sclerosis.* Mult Scler. 2002;8:382-9.

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