Executive dysfunction and cognitive impairment in a large community-based sample with Multiple Sclerosis from New Zealand: A descriptive study

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Abstract

Multiple Sclerosis (MS) is one of the most common chronic diseases of the central nervous system, and in New Zealand an estimated 4000 people are currently affected. This study was conducted to examine executive functioning, memory and general ability in a community-based sample of 95 participants with MS. The sample included those with relapsing–remitting, secondary progressive, chronic progressive and benign MS with an average duration of illness of 11.8 years. Only 9\% of the participants showed no indication of cognitive impairment with most exhibiting mild executive dysfunction across the range of shifting, inhibition, fluency and working memory categories. As this became more widespread, all other measures of cognitive ability and memory also showed evidence of deterioration, but in some, this may have been due to slowed information processing. Overall, there was a high degree of variability in the levels of performance and there was no ‘typical’ pattern of deficits associated with MS. Thus, a proportion of those living with MS may have to cope with noticeable and unpredictable cognitive decline in addition to their physical disabilities.

Keywords: Multiple Sclerosis; Executive functioning; Cognitive ability; Depression; Intelligence; Memory

1. Introduction

Multiple Sclerosis (MS) is an inflammatory disorder of the central nervous system, affecting 2.5 million people worldwide and approximately 4000 within New Zealand. MS is a lifelong illness. Its course differs between individuals, in some it follows a relapsing and remitting course while in others the disease is progressive from outset. The clinical symptoms of the disease are varied, depending on the location of plaques or lesions within the CNS, but can include both physical difficulties (e.g., limb weakness, optic neuritis, incontinence, vertigo, ataxia, facial paralysis, seizures, fatigue) and also cognitive difficulties (e.g., aphasia, poor learning and memory, attention and concentration, mental speed, problem solving and word finding) (Brassington & Marsh, 1998; Henry & Beattie, 2006; Knight, 1992; Parmenter et al., 2007; White, Nyenhuis, & Sax, 1992).

While the physical difficulties of living with MS have been extensively documented, fewer studies have examined the cognitive deficits associated with MS in detail, particularly in patients outside of specialist clinics. It has
been suggested that some degree of cognitive dysfunction can be found in 43–65%, of patients with MS, with severe cognitive dysfunction affecting some 20–30% (DeSousa, Albert, & Kalman, 2002; Parmenter et al., 2007; Rao, 1996). Many individuals that have MS live independently, with limited, if any, access to a specialist clinic. Clearly, cognitive deficits and particularly executive dysfunctions within this population could have a profound impact on their quality of life and would also have implications regarding the provision of appropriate support services.

1.1. General ability

On measures of general ability (e.g., one of the Wechsler Adult Intelligence Scales) the most common pattern of performance reported for individuals with MS, is of a discrepancy between Verbal and Performance IQs, with Performance IQ in some studies being 7–10 points lower (Rao, 1996; White et al., 1992). To some extent this reflects the task demands of Performance Scale subtests, including the timed nature of several subtests, and with some requiring motor dexterity, which is often compromised in MS. For example, performance on the Digit Symbol subtest, which involves motor dexterity and psychomotor speed, is frequently the lowest by individuals with MS and is often significantly lower than controls (Andrade et al., 1999; Klonoff, Clark, Oger, Paty, & Li, 1991; Rao, 1986; Ryan, Clark, Klonoff, & Paty, 1993). Consequently, many researchers choose to use only the Verbal IQ subtests as measures of general ability (McIntosh-Michaelis et al., 1991; Rao, Leo, Bernardin, & Unverzagt, 1991). Even these studies, however, have produced conflicting results, Rao et al. (1991), for example, found significant differences between controls and MS participants in all subtests, while McIntosh-Michaelis et al. (1991) found no significant difference in the Verbal IQs of their MS and control groups and all the age scaled subtest means were within the ‘normal’ range. This again suggests a lack of consistency in impairment of general ability of those with MS, which is likely to reflect the heterogeneity of the disease.

1.2. Memory

For many years the cognitive deficits in MS have been characterised as being similar to subcortical dementia, which implies an impairment in memory recall that can be improved by cuing. Recognition, encoding and storage abilities are generally thought to remain intact, although the profile of cognitive symptoms accompanying MS can be extremely diverse (Fennell & Smith, 1990; Mohr & Cox, 2001; White et al., 1992). For example, some studies indicate that those with MS have deficits in long term memory but performances similar to controls on short term measures, recognition and rate of forgetting (Rao et al., 1991; Rao, Leo, & St. Aubin-Faubert, 1989). In contrast, others have found impairments on tests of immediate recall (verbal and visual), delayed recall, cued recall and recognition measures (Minden, Moes, Orav, Kaplan, & Reich, 1990; Staffen et al., 2002). Rao et al. (1989) cited in Knight (1992), found the largest impairment in the MS populations in immediate and delayed Logical Memory and Visual Reproduction, using the Wechsler Memory Scale (WMS). In contrast, Fischer (1988) found a greater overall degree of memory impairment, as evidenced by significantly lower scores on all subtests of General Memory and Delayed Recall, and lower retention and learning rates compared to controls.

Meta-analyses conducted on these diverse findings found that visual and verbal learning, immediate and delayed recall and recognition are all significantly impaired in MS participants compared to controls (Thornton & Raz, 1997; Wishart & Sharpe, 1997). However, even meta-analyses have failed to reach consistent conclusions with regard to the effects of MS on memory; Zakzanis (2000), for example, concluded from his meta-analysis that although both verbal and non verbal recall tasks showed impairment, recognition remained largely in tact.

1.3. Executive functions

Previous research indicates that 15–20% of individuals with MS have impaired executive functions (Fischer, 2001; Fischer et al., 1994; Rao et al., 1991). As previously mentioned, the cognitive characteristics of MS were considered to resemble those of subcortical dementia, and research measures were selected accordingly. Reasoning ability, assessed by the Halstead Category Test, was the most common measurement of executive integrity. More recently a wider range of tests have been used including the Wisconsin Card Sorting Test (WCST), Oral Word Fluency Test, and Tower of London with deficits found on many of these measures (Beatty, Goodkin, Beatty, & Monson, 1989; Beatty, Hames,
Blanco, Paul, & Wilbanks, 1995; Beatty & Monson, 1996; Caltagirone, Carlesimo, Fadda, & Roncacci, 1991; Denny, Sworowski, & Lynch, 2005; Parmenter et al., 2007; Rolania, Olmos, & Urdiain, 2006). Group data, however, show a high degree of variability, again likely due to the differing symptoms and disease course found in each patient. Studies that examine a broad range of executive functions are rare, and thus, it is hard to draw any firm conclusions as to whether specific types of ‘executive’ deficits are characteristic of MS. In general terms, Rao et al. (1991) suggest that in addition to information processing speed, attention, and conceptual reasoning are compromised in the MS population. Fischer et al. (1994) concur generally with these findings, concluding that ‘known’ deficits in MS include those related to slowed information processing speed, complex attention, and executive functions such as problems solving. Given the complexity of executive functions, and the inconsistencies of previous findings, further studies are needed to clarify the degree and types of executive difficulties experienced by those with MS and the relation between executive dysfunction and other types of cognitive impairment.

1.4. The present study

In summary, in addition to deficits in processing speed, many individuals with MS experience some executive dysfunction and other cognitive impairment, especially memory. However, research findings to date suggest that there are no specific patterns of cognitive or memory deficits reliably associated with the disease. Executive deficits, in particular, are poorly understood in MS, yet these are particularly important for daily functioning and the level of independent living arrangements possible for people diagnosed with MS. The aim of the present study was to conduct a systematic and comprehensive assessment of executive functioning, general cognitive ability and memory, in a large community-based sample of individuals diagnosed with MS. Unlike previous studies we assessed a wide range of executive abilities by using the Delis–Kaplan Executive Function System (DKEFS; Delis, Kaplan, & Kramer, 2001) which includes tests sensitive to shifting, or mental flexibility, fluency, planning, reasoning and abstract thinking accompanied by extensive normative data from a sample of 1750 individuals. Thus it was possible to examine whether there is a systematic pattern to executive performance in our MS sample, and how this related to other cognitive abilities.

2. Method

2.1. General methodological approach

In order to determine if certain cognitive deficits are associated with a particular disorder, there are broadly two different approaches which can be taken. Firstly, the participants’ current scores can be compared to that of a control group or standardised norms associated with the neuropsychological tests. Alternatively, the participants’ current score can be compared to their own pre-morbid score or an estimate of their own pre-morbid ability (Spreen & Strauss, 1998). There are disadvantages associated with each of these approaches. For example, Lezak et al. (2004) suggest that comparisons with normative standards are “appropriate only when the function or skills or capacity that is being measured is well within the capability of all intact adults and does not vary greatly with age, sex, education, or general mental ability” (p. 89). Furthermore, they recommend that when trying to assess whether or not an individual has suffered a decline in cognitive abilities that are normally distributed in the adult population, comparisons should be made with the individual’s pre-morbid score (either known or estimated). This approach avoids classifying those with, for example, low current IQ scores as having deficits when their pre-morbid functioning was also low (Lezak et al., 2004). It also enables identification of deficits in individuals who performed at a very high level pre-morbidly, whose performance has dropped significantly but still falls in the average range.

Ideally each individual’s score would be compared to their ‘known’ level of pre-morbid functioning. However, in the case of adult onset brain disorders, this information is rarely available. Therefore, more often than not, an individual’s level of pre-morbid functioning has to be estimated. Vocabulary-based tests have been used for this purpose, as this aspect of functioning is believed to be reasonably resilient to mental deterioration. Tests based on reading phonetically irregular words have also been developed to improve the accuracy of prediction. These predictions are most accurate for VIQ and FSIQ (Lezak et al., 2004).

In the following study the cognitive effects of MS were evaluated in a large sample of individuals with MS using the method to identify deficit advocated by Lezak et al. (2004) described above.
2.2. Participants

Ninety-five community-based individuals with MS from the greater Waikato region of New Zealand participated in this study. A total of 98 participants were originally recruited, but 3 were subsequently excluded, 1 due to an aneurysm, 1 for epilepsy and 1 for malingering. This sample makes up approximately 2.5% of the population of MS sufferers in New Zealand.

Participants were aged between 17 and 78 years, with a mean age 52.6 years (S.D. = 11.4), and the majority (64) were between 40 and 60 years old. A total of 75 (78.9%) participants were female and 20 (21.1%) were male. The average number of years of education was 12.9 years (S.D. = 3.1, range 9–27 years). All participants’ first language was English. Approximately one third of participants, 31 (32.6%), classified themselves as retired, 25 (26.3%) were in paid employment, 20 (21.1%) were sickness beneficiaries, 15 (15.8%) classified themselves as homemakers, and 2 (2.1%) were unemployed and the same number were students.

The average number of years since the participants detected the first symptoms of MS was 24.2 years (S.D. = 13.0; range 2.0–61 years), with the majority (75) falling within the relatively wide time frame of 10–38 years. In contrast to the number of years since first symptom detection, the average number of years since MS was first diagnosed was 11.8 years (S.D. = 10.4, range .5–48 years). The classification of disease course showed a predictable split. Forty-seven individuals (49.5%) had the relapsing–remitting form of MS, 30 (31.6%) had acute or secondary progressive, with only 15 (15.8%) indicating they were chronic progressive and very few, 3 (3.2%) indicating the benign form. At the time of testing all relapsing–remitting participants self-reported that they were in remission. Approximately one third, 32 (33.7%) did not take any medication but the majority, 63 (66.3%) were taking some form of medication, however the details of this were not provided by all participants.

2.3. Materials

2.3.1. Screening measures

2.3.1.1. Chicago Multiscale Depression Inventory (CMDI) (Nyenhuis et al., 1998). This measure of depressive tendencies was specifically developed for use in medical patients who show symptoms of depression (e.g., fatigue) as part of their medical condition. It has three subscales: a mood scale (e.g., items such as ‘sad’, ‘glum’ and ‘low’), an evaluative scale, (e.g. items such as ‘punished’ and ‘resented’), and a vegetative scale, (e.g., items such as ‘unable to pay attention’, ‘exhausted’ and ‘sluggish’), in addition to a composite score. Respondents rate each of 50 items on a Likert scale of 1 (‘not at all’) to 5 (‘extremely’), based on the past week.

Normative data for this assessment showed high internal consistency (alpha coefficients ranged from .77 to .91), and its validity has been demonstrated by significant correlations with the Beck Depression Inventory, Profile of Mood Scales and the Geriatric Depression Scale (Nyenhuis et al., 1998). This measure was thought to be most suitable for this sample as it provides a measure of depression which is not confounded by MS symptoms.

2.3.1.2. Kurtzke Expanded Disability Status Scale (EDSS) (Kurtzke, 1983). This scale is the most widely used measure of physical disability within the MS population. It ranges from 0 (normal), and progresses in .5 increments, to 10, which is death. Ratings between 0 and 5.0 relate to those who are fully ambulatory, while ratings from 5.5 upwards relate to the ability to ambulate. Guidelines accompanying the scale indicate the usual functional capacity related to each level.

2.3.1.3. Wechsler Test of Adult Reading (WTAR; Wechsler, 2001). This test allows researchers to calculate estimates of pre-morbid WAIS-III IQ and Index scores, and WMS-III Index scores. As this study had no control group, this measure was selected primarily because it is co-normed with the WAIS-III and WMS-III batteries, and is considered to be most useful for educated White populations with IQ’s within the average range (Ginsberg, 2003). Test–retest reliability coefficients for each age group are high, ranging from .92 to .94, and its strongest relationships are with the Wide Range Achievement Test (WRAT-R) Reading ($r = .73$), WAIS-III Verbal IQ ($r = .75$) and American National Adult Reading Test (AMNART) ($r = .90$). Its relationships with the WAIS-III Performance IQ ($r = -.59$), and the Memory Indices from the WMS-III (Immediate Memory, $r = .47$, General Memory, $r = .49$, and Working Memory, $r = .51$) are considerably weaker. Overall, the prediction intervals for this test are quite large, but compared to other tests of pre-morbid intelligence, the standard error of the estimate of the WTAR predicted score for the WAIS-III FSIQ
(10.3), is in the mid range (Ginsberg, 2003). Given its extensive norms and reasonable accuracy of estimation, this test was selected as the measure of pre-morbid level of ability. The test requires participants to read aloud 50 words that are presented on a card. Scores from this test are converted into estimates of pre-morbid IQ/memory, which, by comparison with current scores, allows the researcher to determine the long-term effects of MS.

2.3.2. Cognitive and memory assessment

2.3.2.1. Wechsler Adult Intelligence Scales-III (WAIS-III; Wechsler, 1997a). The WAIS-III was used to assess general cognitive ability, as it provides a broad overview of general ability, and along with its earlier versions has been widely used in a variety of clinical populations, including those with MS (e.g., Andrade et al., 1999; Clemmons, Fraser, Rosenbaum, Getter, & Johnson, 2004; Klonoff et al., 1991). It provides extensive normative data (Wechsler, 1997a. Administration and Scoring Manual) and has become well accepted over a considerable period of time. Internal consistency and test–retest reliability coefficients range from the .70s to the .90s, and its validity has been established through similarly high correlations with the WAIS-R and the WIAT.

From this battery, standardised age-appropriate scaled scores for each of 14 subtests are generated. Four Index scores are derived from 11 of these subtests; Verbal Comprehension Index (VCI), Perceptual Organisation Index (POI), Working Memory Index (WMI) and Processing Speed Index (PSI). In addition, Verbal IQ (VIQ), Performance IQ (PIQ) and Full Scale IQ (FSIQ) scores can be derived from a slightly different combination of 11 subtests.

2.3.2.2. Wechsler Memory Scale-III (WMS-III; Wechsler, 1997b). Memory functions were assessed via the WMS-III. Similar to the WAIS-III, this battery was chosen as it is well accepted and widely used measure of memory functioning, and an earlier version has been shown to be sensitive to memory deficits in those with MS (e.g., Clemmons et al., 2004; Fischer, 1988). It also provides considerable normative data across a range of ages (Wechsler, 1997b. Administration and Scoring Manual).

Reliability coefficients for internal consistency range from the .70s to the .90s, and for test–retest reliability in the .60s and .70s. Coefficients relating the WMS-III to the WMS-R and the Wechsler Individual Achievement Test (WIAT) were variable but provided evidence for convergent and divergent validity. In addition to the age-scaled scores for each subtest, seven summary Index scores are derived from the subtests scores; Auditory Immediate, Visual Immediate, Immediate Memory, Auditory Delayed, Visual Delayed, Auditory Recognition Memory, General Memory (Delayed) and Working Memory.

2.3.2.3. Delis–Kaplan Executive Function System (Delis et al., 2001). The DKEFS is a relatively new assessment battery, which uses standardised versions of several currently used tests to assess a wide range of executive functions. The norms are derived from a large sample which is comparable to the normative samples of the WAIS-III and the WMS-III (DKEFS Examiners Manual, 2001). Although it is relatively new, some of the tests have been used to assess executive functions in the MS population (e.g., Beatty et al., 1995; Parmenter et al., 2007). In addition, a list of validity studies which have demonstrated the sensitivity of the DKEFS to executive function deficits in a variety of clinical populations has recently been published by Delis, Kramer, Kaplan, and Holdnack (2004). Although reliability coefficients for the DKEFS tests were generally less than .80, this is comparable with other neuropsychological tests, and it is probable that for these assessments, test complexity underlies performance variability. Thus, this battery was selected as it assesses a wide range of executive functions using tasks that have been shown to be valid and reliable.

The DKEFS comprises nine tests, which are adaptations of tests currently used for assessing executive functions. These tests are, Trail Making, Verbal Fluency, Design Fluency, Colour Word Interference, Card Sorting test, 20 Questions, Word Context, Tower Test and Proverbs. These 9 subtests provide information regarding a wide range of executive abilities, and provide 20 primary scores, each with a mean standardised score of 10, standard deviation of 3. Although working memory processes are utilized when performing these tests, working memory is not directly assessed in this battery.

2.4. Procedure

Ethical approval for this research was obtained from the Psychology Research and Ethics Committee at the University of Waikato. Individuals with a diagnosis of MS who belonged to the local MS society were sent an information letter and contacted the researcher directly if they were interested in taking part in the research. The same information
The assessments were carried out over two 3-hour sessions. The first session comprised a brief overview of the research and the assessments to be carried out, followed by the WMS-III. Following a break, the Expanded Disability Status Scale rating was estimated, and the following measures were administered: WTAR, Chicago Multiscale Depression Inventory and the WAIS-III. The second session began with assessment of attention and information processing speed (results reported elsewhere, Drew, 2005), followed by administration of the DKEFS battery. The second session was completed with an assessment of daily functioning, and judgement of temporal events (results reported elsewhere, Drew, 2005). The time between the first and second sessions varied but the average interval was 12 days (minimum 2 days, maximum 2 months). The time between assessment sessions did not appear to influence the outcome of the assessment as there were no significant correlations between the number of interim days and second session performance levels. All participants with relapsing–remitting MS, self-reported that they were in remission at the time each assessment was conducted.

3. Results

3.1. Screening measures

3.1.1. Chicago Multiscale Depression Inventory

The standardised scores for this measure are based on a sample of 420 adults demographically matched to the 1980 US census figures. Each subscale has a standardised mean of 50 and a standard deviation of 10. The sample composite mean score for the CMDI was 54.7 (S.D. = 13.1, range 36.0–103.0). The majority of the scores were in the 40s and 50s, indicating that there was little evidence of depression in the sample. The mean scores of the Mood Subscale (M = 50.9, S.D. = 11.9, range = 39.8–92.3) and the Evaluative Subscale (M = 52.0, S.D. = 12.8, range = 44.0–112.0) were consistent with this, but the Vegetative Subscale had a slightly higher mean of 58.7 (S.D. = 13.2) and an extensive range (33.8–91.8). As the Vegetative subscale addresses such issues as fatigue and ability to concentrate, which are common symptoms of MS, the higher mean value in that subscale, should be attributed to MS rather than depression per se. Participants scoring at or above the 75th percentile on the CMDI were compared with those scoring at or below the 50th percentile using an independent groups t-test (Arnett, Higginson, Voss, Bender, et al., 1999; Arnett, Higginson, Voss, Wright, et al., 1999). Those with higher CMDI scores obtained a significantly lower score on the Processing Speed Index (t(65) = 2.26, p = .03). Further analysis revealed that this was due primarily to a significant difference between those scoring high and low on the mood subscale (t(65) = 2.19, p < .05). As the influence of depression on cognitive ability scores appeared to be limited to the processing speed index of the WAIS-III, it was not taken into account for subsequent analyses.

3.1.2. Kurtzke Expanded Disability Status Scale

The mean score for the sample on the EDSS was 4.8 (S.D. = 2, range 1–8) which falls between level 4.5 (‘Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; able to walk without aid or rest some 300 m.’) and level 5.0 (‘ambulatory without aid or rest for about 200 m; disability severe enough to impair full day activities, e.g. to work a full day without special provisions’) (see scoring guidelines, Kurtzke, 1983). The distribution of scores was actually bimodal, peaking at level 3 and level 6. This, indicated that although approximately half the sample had only minimal levels of physical disability, there was an almost equally large number whose physical disabilities were more severe, which may influence scores on tests requiring some degree of manual dexterity.

3.1.3. Wechsler Test of Adult Reading

The mean score of the sample on the Wechsler Test of Adult Reading test was 106.0 (S.D. = 11.6, range 68–123). For all but four participants the WTAR scores alone were used to predict the scores. For the remaining 4 participants, their WTAR plus demographic predicted WTAR score was more than 19 points higher than their actual WTAR score, therefore WTAR plus demographic details were used to predict both the WAIS-III and the WMS-III scores (as recommended on the WTAR score sheet). The mean WTAR predicted Full Scale IQ (FSIQ) score was 103.9 (S.D. = 8.6, range 80–123). Based on the predicted scores, only three participants scored lower than
1 S.D. below the standardised mean of the WAIS-III (<85), while five participants had predicted scores greater than 1 S.D. above the mean (>115). This indicated that the majority of participants (86) fell within the normal IQ range, however 10 participants had a predicted FSIQ score of 114 and a significant proportion (71%) obtained predicted IQ scores higher than the standardised mean (100), suggesting above average levels of pre-morbid intelligence.

A significant relationship was found between the number of years education and both the WTAR scores ($r = .218$, $p = .035$) and the WTAR predicted FSIQ scores ($r = .498$, $p < .01$). The correlation between years of education and WTAR scores is quite low, which suggest that for this sample, years of education are not an accurate predictor of ability. This could be due to the wide range of years of education, or the older participants may have left school for other reasons, rather then having reached their full potential.

### 3.2. Cognitive and memory assessment

#### 3.2.1. General cognitive ability

Because of the physical limitations that characterised some of the participants with MS, not all participants were able to complete the full compliment of Performance subtests on the WAIS-III. All but one participant, however, completed sufficient subtests to enable a Performance IQ score to be calculated.

The means and 95% confidence intervals for each WAIS-III index and IQ score are illustrated in Fig. 1. This shows that the scores of this sample were close to the standardised mean (100) for most of the seven measures. The one exception was the Processing Speed Index whose mean score was up to 10 points lower than the other indices.

Thus the mean scores for this sample suggest there was no overall impairment in this sample of individuals with MS in general cognitive ability. The mean Full Scale IQ of 100.2 was also similar to the mean pre-morbid IQ score prediction of the Wechsler Test of Adult Reading from the pre-assessment (103.9). When the detrimental impact of possible physical limitations on the Performance Indices was considered, this would suggest that there has been very little decline in general ability in this sample as a whole.

In order to determine the effects of MS on general ability, scores for each index and IQ measure making up the WAIS-III were compared with their WTAR predicted scores. The actual numbers of participants who scored significantly lower (as per WTAR manual) than their WTAR predicted scores are presented in Table 1. From this it can be seen that more participants had significantly lower than predicted scores on the Performance IQ (37) compared to the Verbal IQ (25) even though this was not apparent in the data presented in Fig. 1. However, the 47 participants (50%) who scored significantly below their predicted level on the Processing Speed Index which contributes in part to the Performance

![Fig. 1. Means (and 95% confidence intervals) of the WAIS-III indices.](image)
Table 1
Number and percentage of participants whose scores were significantly lower than predicted for each WAIS-III index and IQ measure

<table>
<thead>
<tr>
<th>WAIS-III index</th>
<th>Current score less than predicted (N)</th>
<th>Current score less than predicted (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal Comprehension</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>Perceptual Organisationa</td>
<td>31</td>
<td>33</td>
</tr>
<tr>
<td>Working Memory</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>Processing Speedb</td>
<td>47</td>
<td>50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IQ measures</th>
<th>Current score less than predicted (N)</th>
<th>Current score less than predicted (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal IQ</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>Performance IQa</td>
<td>37</td>
<td>39</td>
</tr>
<tr>
<td>Full Scale IQa</td>
<td>35</td>
<td>37</td>
</tr>
</tbody>
</table>

Note. Verbal IQ is made up of the Verbal Comprehension Index and the Working Memory Index. Performance IQ is made up of the Perceptual Organisation Index and the Processing Speed Index. Full Scale IQ is the aggregate of the Performance IQ and the Verbal IQ.

a $N=94$.
b $N=86$.

IQ, could have contributed substantially to this difference as this index includes a substantial motor skill component. Given this confound, examination of performance on the Perceptual Organisation Index and Verbal Comprehension Index, is probably a more realistic indication of the relative prevalence of impairment in the perceptual versus verbal domains. However, the numbers showing significant differences on these index scores still suggest that performance in the perceptual domain is weaker than in the verbal domain in this sample. This comparison still has its limitations as two of the subtests contributing to Perceptual Organisation Index are timed, and one (Block Design) may also be affected by physical slowing.

Detailed comparisons of the predicted WAIS-III scores and actual scores revealed that 47 (50.51%) participants obtained WTAR predicted Verbal IQ, Performance IQ, and/or Full Scale IQ scores which were significantly higher (as per the WTAR tables) than their actual score. Of these 47 participants, 16 (34.04%) scored significantly lower than predicted on all three indices, the majority, 22 (46.81%), scored significantly lower on the Performance IQ or both Performance IQ and Full Scale IQ, and only 9 (19.15%) scored significantly lower on their Verbal IQ or both Verbal IQ and Full Scale IQ. In contrast to the Wechsler Adult Intelligence Scales scores, these data suggest that there may have been some decline in general intelligence performance, at least in those 25 participants whose actual scores were significantly lower than predicted in either all three WAIS-III indices, or in the Full Scale IQ and/or the Verbal IQ measures. For the 22 participants whose current scores were significantly lower for Performance IQ only, this may have been, at least in part, due to disease related physical slowing, rather than a decrement in cognitive performance. Even so, for many of these cases their scores remain within the normal range.

In an attempt to identify groups of participants with similar patterns of impairment, a cluster analysis was conducted based on the Verbal Comprehension Index, the Perceptual Organisation Index and the Working Memory Index. The Processing Speed Index was not included in this analysis because of the amount of missing data and its dependence on motor skills. Two main clusters were found that correctly grouped 95.8% of the data, and the mean Index scores (including the Processing Speed Index) for each cluster are shown in Fig. 2.

This figure shows that the 57 participants (61% of the sample), in cluster 1, had mean Index scores which showed little variability between them and which were all above the standardised mean. However, comparisons with WTAR predicted scores indicated that 15 of these participants (26% of the cluster) had scored significantly lower than predicted. The majority of these (10, 18% of the cluster) scored significantly lower on Performance IQ or PIQ and FSIQ, and 3 (5% of the cluster) had significantly lower Verbal IQ or VIQ and FSIQ scores. Of these 15 participants in cluster 1, only 6 had actual FSIQ scores less than 100, and these were all in the 90s.

Cluster 2, which included the remaining 37 (39%) participants had mean Index scores that were all below the standardised mean of 100, but only the Processing Speed Index was more than 1 S.D. below this mean (<85), suggesting little if any clinical impairment. However, of the 37 participants that made up this cluster, 30 (81%) had index scores that were significantly lower than their WTAR predicted score. Fourteen (38% of the cluster) scored significantly lower on all indices, 11 (30% of the cluster) scored significantly lower on the Performance IQ or both Performance IQ and FSIQ, but only 5 (13% of the cluster) had lower Verbal IQ or VIQ and FSIQ scores. In comparison with cluster 1, only
Fig. 2. Clusters of participants based on the Verbal Comprehension, Perceptual Organisation and Working Memory Indices of the WAIS-III.

One participant in cluster 2 had a FSIQ score over 100. However, the most notable difference between the two clusters was that for cluster 1, no participants scored significantly lower than predicted on all indices.

As the sample in this study was community based, the participants presented with a wide range of demographic and clinical characteristics. A number of linear regression analyses were therefore conducted to determine the effects of age, years of education, years since MS was diagnosed, and years since first symptoms were experienced on the Verbal Comprehension Index, the Perceptual Organisation Index, the Working Memory Index, the Processing Speed Index, the VIQ and the PIQ. Of these, the only significant relationship was found between years of education and the Verbal Comprehension Index ($R^2 = .24$, $p < .001$), the VIQ ($R^2 = .17$, $p < .001$) and the POI ($R^2 = .05$, $p < .05$). A MANOVA comparing VCI, POI, WMI and PSI scores across disease types was not significant ($p > .05$), indicating that general ability scores did not differ significantly between the various types of MS.

With regard to EDSS scores and general cognitive ability, those with deterioration on the greatest number of WAIS-III indices (4) are predominantly classified as having a high degree of physical disability (see Table 2). In addition, twice as many participants with no deterioration on their WAIS Index scores have low physical disability compared to high levels of physical disability, but there is no clear relationship between level of physical disability and the intermediate levels of decline in general ability. However, many of these ‘deteriorated’ scores were due to deficits on the Processing Speed Index. If the PSI is not considered, it is only those participants (12) with deterioration in all three indices where the majority (8) also have high levels of physical disability. Chi square tests of Independence for both analyses were not statistically significant ($p > .05$), supporting the indications that higher levels of physical disability are not necessarily indicative of cognitive deficits in this instance.

Table 2

<table>
<thead>
<tr>
<th>WAIS impaired scores (no.)</th>
<th>Low physical disability ($N$)$^a$</th>
<th>High physical disability ($N$)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PSI included</td>
<td>PSI excluded</td>
</tr>
<tr>
<td>0</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>1</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

PSI: Processing Speed Index.

$^a$ EDSS $\leq 4.5$.

$^b$ EDSS score $> 4.5$. 
3.2.2. **Memory**

All participants (95) were able to complete this assessment. The sample means and 95% confidence intervals for the various WMS-III indices are presented in Fig. 3.

3.2.3. **Assessment of immediate and delayed learning and recall**

For the group as a whole it seemed that there was no significant impairment in any of the domains of memory assessed as none of the index means were lower than 1 S.D. (15) below the mean of the standardised data (100). It is, however, evident that both visual indices, Visual Immediate (89.03) and Visual Delayed (88.68), were lower than the comparable auditory scores (94.55 Auditory Immediate and 94.62 Auditory Delayed), and a greater variance within the visual indices (S.D. = 16.89 Visual Immediate and 15.72 Visual Delayed) is also observed. Paired sample t-tests confirmed significant modality (visual versus auditory) differences, for both Visual and Auditory Immediate indices, \( t(94) = 4.098, p < .001 \) and Visual and Auditory Delayed Indices, \( t(94) = 5.022, p < .001 \). No significant difference was found between the disease types and the Memory Index scores.

In order to determine the effects of MS on memory functioning, scores for each of the three main WMS-III indices (Immediate, General and Working Memory) were compared with the WMS WTAR predicted score for each participant, to determine the numbers of individuals who scored significantly below their WTAR predicted score (as per WTAR tables) on one or more of the WMS-III indices. Again, predicted scores for all but four participants were based on WTAR scores alone. For the remaining four participants, WTAR plus demographics were used as recommended by the scoring sheet. Although it is acknowledged that the WTAR predicted WMS Index scores are not as accurate as those predicted for the WAIS-III, it was felt for this measure, that predicted scores would more closely approximate each individual’s expected performance level than the more generalized normative data. These data are presented in Table 3.

From Table 3, it can be seen that the number of participants whose scores were significantly below their predicted score ranged from 31 (33.3%) for the Working Memory Index to 56 (60.2%) for the General Memory Index. Thus, the numbers of participants scoring significantly below their predicted level were considerably greater than had been suggested by the sample means. It was also apparent that considerably fewer participants had actual scores that were

<table>
<thead>
<tr>
<th>WMS-III Index</th>
<th>Current score less than predicted (N)</th>
<th>Current score less than predicted (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Memory</td>
<td>51</td>
<td>54.8</td>
</tr>
<tr>
<td>General Memory</td>
<td>56</td>
<td>60.2</td>
</tr>
<tr>
<td>Working Memory</td>
<td>31</td>
<td>33.3</td>
</tr>
</tbody>
</table>
significantly lower than their predicted score on the Working Memory measure compared to the General Memory Indices.

Cluster analysis was again conducted to group those participants with similar patterns of memory scores. Using the composite Immediate Memory (Auditory Immediate and Visual Immediate), General Memory (Auditory Delayed, Visual Delayed and Recognition) and Working Memory Indices, both the three and four cluster solutions correctly classified 95.8% of the participants. However one cluster in the four cluster solution included only four participants therefore the three cluster solution was considered optimal. The means of all six index scores for each of the three clusters are shown in Fig. 4.

Fig. 4 illustrates that cluster 1 (N = 31), has mean memory scores which are all well above the standardised mean of 100. These participants also have the least variability between their mean Index scores and show little evidence of an auditory/visual differential. Seven of these participants did however have WAIS-III scores which were significantly below their WTAR predicted scores, but only two participants in this cluster were in the WAIS-III cluster with the lower scores (see Fig. 5).

Although the mean Memory Index scores of cluster 2 (N = 41) were lower than those of cluster 1, none were more than 1 S.D. below the standardised mean (< 85). However, when compared with cluster 1, more variability was seen across the mean Index scores and some auditory/visual differential was evident (Fig. 4). Nineteen participants in this cluster had WAIS-III scores significantly lower than their WTAR predicted scores, and 11 of these 19 were in the WAIS-III cluster with the lower scores. Overall 26 participants from this cluster were in the WAIS-III cluster with the higher scores (Fig. 5).

In contrast to the previous two clusters, all of the mean Index scores of cluster 3 (N = 23) were lower than 1 S.D. below the standardised mean (Fig. 4). This cluster was also characterised by the most pronounced auditory/visual differential, and 19 (83% of the cluster) had WAIS-III scores that were significantly lower than their WTAR predicted scores. From this cluster all but two participants were in the WAIS-III cluster with the lower scores (Fig. 5).

There was no significant relationship between scores on the WMS-III and years of education, symptom duration or time since diagnosis. Nor did scores differ across the disease sub types.

3.3. Executive functions

3.3.1. Delis–Kaplan Executive Function System

The means and variability measures of the 20 primary scores of executive functioning derived from the DKEFS are presented in Table 3.

An attempt was made to link each of these scores to one of the following executive function categories Shifting, Inhibition, Planning, Reasoning/Problem Solving, Fluency and Working Memory. This was to provide a ‘behavioural’ description of the results of the neuropsychological assessment, although it is acknowledged that one-to-one mapping
of each test onto a single category was difficult since many tests are multi-faceted. In these cases the test was assigned to the category that best described its main purpose. As no separate measures of working memory could be obtained from the DKEFS, the scores from the Working Memory Index of the WMS-III were used to examine this category of executive functioning.

The mean scores in Table 4 show that the group of participants as a whole performed around the reported standardised means for the test. These data might suggest that, as a whole, these MS participants are relatively free of executive function impairment. However, the large standard deviations, and range of scores suggest that this may not be an accurate portrayal of this population. For subsequent analysis, consideration was given to estimating pre-morbid executive function based on the WTAR scores, but as there were no significant relationships between WTAR scores and the DKEFS, this approach was considered inappropriate. Thus, each individual’s current DKEFS scores were compared to the standardised means. Following this, it became clear that a large proportion of individuals were scoring more than 1 S.D. below the standardised mean on a number of DKEFS tasks.

Table 3 shows that the number of participants scoring 1 S.D. below the standardised mean was greatest for the Fluency Switching (score 4), followed by Colour Word Inhibition (score 6) and Colour Word Switching (score 7), then Trails number-letter switching (score 1), and Letter Fluency (score 2). As their names suggest, these tests predominantly assess executive functions such as fluency, shifting, and inhibition. In contrast the proverbs scores, excluding the abstraction measure (scores 16–19), the 20 Questions Abstraction and Total scores (scores 11 and 12), along with Design Fluency (score 5) and Word Context (score 14) had the fewest number of participants with scores lower than 1 S.D. below the standardised mean, suggesting that general executive function and reasoning abilities were somewhat less affected in this sample.

When examining these 20 primary DKEFS scores on a case-by-case basis, 32 (34%) participants scored higher than 1 S.D. below the standardised mean on all measures. Of the remaining 63 (66%) the majority (47) scored lower than 1 S.D. below the standardised mean on fewer than 6 measures, with most of these only scoring lower than that level on 1 (20 participants), or 2 (11 participants) tasks. The remainder (16) showed impairments on anywhere between 6 (2 participants) and 19 scores (1 participant). Thus, this suggests that approximately 17% of the MS sufferers had widespread difficulties with executive functioning. In addition, closer examination of the lower scores failed to reveal any consistent weaknesses in executive functioning in those with MS. That is, MS sufferers were not characterised by lower scores in specific categories of executive functioning, indeed the opposite was true, with weaknesses apparent across the categories of shifting, fluency, inhibition and reasoning.
Table 4
Means, standard deviations, range and number of participants scoring lower than 1 S.D. below the standardised mean for each of the 20 primary DKEFS Tests including the appropriate executive category

<table>
<thead>
<tr>
<th>DKEFS test</th>
<th>Mean</th>
<th>S.D.</th>
<th>Range</th>
<th>Scoring &lt;85 (N)</th>
<th>Executive category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Trails Switching</td>
<td>8.5</td>
<td>3.9</td>
<td>13</td>
<td>22</td>
<td>Shifting</td>
</tr>
<tr>
<td>2. Letter Fluency</td>
<td>10.1</td>
<td>4.1</td>
<td>17</td>
<td>21</td>
<td>Fluency</td>
</tr>
<tr>
<td>3. Category Fluency</td>
<td>10.2</td>
<td>3.7</td>
<td>18</td>
<td>15</td>
<td>Fluency</td>
</tr>
<tr>
<td>4. Switching Fluency</td>
<td>8.9</td>
<td>3.8</td>
<td>18</td>
<td>26</td>
<td>Shifting</td>
</tr>
<tr>
<td>5. Design Fluencya</td>
<td>10.5</td>
<td>3.2</td>
<td>15</td>
<td>9</td>
<td>Fluency</td>
</tr>
<tr>
<td>6. Colour Word Inhibition</td>
<td>8.8</td>
<td>3.6</td>
<td>14</td>
<td>24</td>
<td>Inhibition</td>
</tr>
<tr>
<td>7. Colour Word Switching</td>
<td>8.8</td>
<td>3.8</td>
<td>14</td>
<td>24</td>
<td>Shifting/Inhibition</td>
</tr>
<tr>
<td>8. CCST Correct Sorts</td>
<td>9.9</td>
<td>3.0</td>
<td>16</td>
<td>13</td>
<td>Reasoning/Problem Solving</td>
</tr>
<tr>
<td>9. CCST Description</td>
<td>9.7</td>
<td>3.0</td>
<td>17</td>
<td>14</td>
<td>Reasoning</td>
</tr>
<tr>
<td>10. CCST Recognition</td>
<td>9.6</td>
<td>2.8</td>
<td>15</td>
<td>12</td>
<td>Reasoning</td>
</tr>
<tr>
<td>11. 20 Questions Abstraction</td>
<td>10.4</td>
<td>2.9</td>
<td>14</td>
<td>8</td>
<td>Reasoning</td>
</tr>
<tr>
<td>12. 20 Questions Total</td>
<td>10.2</td>
<td>3.5</td>
<td>14</td>
<td>11</td>
<td>Reasoning/Planning</td>
</tr>
<tr>
<td>13. 20 Questions Achievement</td>
<td>9.7</td>
<td>3.5</td>
<td>14</td>
<td>16</td>
<td>Reasoning</td>
</tr>
<tr>
<td>14. Word Contextb</td>
<td>9.7</td>
<td>2.7</td>
<td>14</td>
<td>10</td>
<td>Reasoning</td>
</tr>
<tr>
<td>15. Tower Total</td>
<td>10.0</td>
<td>3.1</td>
<td>16</td>
<td>13</td>
<td>Planning/Inhibition</td>
</tr>
<tr>
<td>16. Proverbs Total</td>
<td>10.4</td>
<td>2.5</td>
<td>11</td>
<td>8</td>
<td>General</td>
</tr>
<tr>
<td>17. Common Proverbs</td>
<td>10.4</td>
<td>2.7</td>
<td>12</td>
<td>10</td>
<td>General</td>
</tr>
<tr>
<td>18. Uncommon Proverbs</td>
<td>10.4</td>
<td>2.5</td>
<td>10</td>
<td>7</td>
<td>Reasoning</td>
</tr>
<tr>
<td>19. Proverbs Accuracy</td>
<td>10.4</td>
<td>2.3</td>
<td>11</td>
<td>6</td>
<td>General</td>
</tr>
<tr>
<td>20. Proverbs Abstraction</td>
<td>10.0</td>
<td>2.7</td>
<td>11</td>
<td>13</td>
<td>Reasoning</td>
</tr>
</tbody>
</table>

CCST: California Card Sorting Test.

a $N=93$.
b $N=94$.

In order to identify common patterns of performance levels over this range of executive functions, a cluster analysis was again conducted. However, in this instance no meaningful differentiation between groups was evident.

3.3.2. Working memory

In this sample 34% of the participants had problems with working memory, a component of executive functioning. When scores were examined on an individual basis, only one participant had an actual working memory score that was significantly lower than their predicted score, while scoring higher than 1 S.D. below the standardised mean on all DKEFS scores.

3.3.3. Physical disability and executive functioning

Given the bimodal nature of the level of physical disability within this sample (as shown by the data from the EDSS), a frequency count was conducted to determine number of participants with high or low levels of physical disability (high = EDSS score > 4.5, low = EDSS ≤ 4.5) in relation to the number of deteriorated scores on the DKEFS. These data are shown in Table 5. It can be seen that those with high levels of physical disability do not all have high

Table 5
Level of disability and number of participants with impaired DKEFS scores

<table>
<thead>
<tr>
<th>DKEFS impaired scores (no.)</th>
<th>Low physical disability (N)a</th>
<th>High physical disability (N)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>&gt;6</td>
<td>7</td>
<td>21</td>
</tr>
</tbody>
</table>

a EDSS ≤ 4.5.
b EDSS score > 4.5.
levels of executive dysfunction. However, three times as many participants with no scores less than 1 S.D. below the standardised mean were in the low physical disability category, and conversely three times as many participants with 6 or more scores less than 1 S.D. below the standardised mean were in the high disability category. Indeed, a Chi squared test of independence ($\chi^2(6, N=95) = 15.23, p < .05$) was significant, suggesting a link between physical disability and executive function decline in MS. In order to explore this relationship further, linear regression analyses were conducted between the EDSS scores and the DKEFS measures. Results showed that the level of physical disability was significantly related ($p < .05$) to all but the Colour Word Inhibition/Switching, and 20 Questions Abstraction scores. $R^2$ values ranged from .15 (Tower Test), .13 (Design Fluency) and .12 (Trails Switching) down to .05 for the Letter Fluency, Switching Fluency, Word Context and Proverbs Accuracy. Although this suggests a general link between physical disability and executive functioning for those in this MS sample, the relationship was stronger for those tests which required some manual dexterity. However, overall the percentage of the variance in the DKEFS scores explained by the physical disability measure was low.

DKEFS scores were not related to age, years of education, years since MS diagnosis or years since symptoms were first experienced. Nor were there significant differences in DKEFS scores across the disease types.

To explore the patterns of cognitive performance associated with MS more thoroughly, WMS-III and WAIS-III cluster membership was examined for those with 0 to 6+ scores lower than 1 S.D. below the standardised mean on the DKEFS measures. The results are illustrated in Fig. 6.

It can be seen from Fig. 6 that while there is no clear pattern in relation to levels of performance, those with 0–3 low scores on the DKEFS came predominantly from the higher scoring WAIS-III cluster (cluster 1), and were relatively evenly divided between the highest and middle scoring WMS-III clusters (clusters 1 and 2). For those with 4 or more lower DKEFS scores the proportion of those in the lower scoring WAIS-III cluster (cluster 2) increased, as did the numbers that were in the lowest scoring WMS-III cluster (cluster 3). Those scoring at a low level on 6 or more DKEFS
measures came exclusively from the lowest scoring WAIS-III cluster and predominantly from the lowest scoring WMS-
III cluster. This suggests that while general ability and memory performance can occur at a different level to executive
functioning in MS, for those with six or more low DKEFS scores, general ability and memory performance also tended
to be low.

A more specific frequency count revealed that of the 16 participants with low scores on a wide range of executive
functions (more than 5 primary DKEFS scores), 13 had lower than predicted scores on all three of the Wechsler Memory
Indices (including Working Memory). Of these 13 participants, all had actual scores that were more than 1 S.D. below
the standardised mean (<85) on all three indices. However, analysis failed to reveal any consistent profile with regard
to patterns or types of impairment in either categories of executive dysfunction, or type of memory impairment in those
with MS.

In relation to general ability, 7 of the 16 participants with low scores on a range of DKEFS measures, scored
significantly below their predicted scores on all three IQ measures (PIQ, VIQ and FSIQ). However, only three of
these had actual scores that were more than 1 S.D. below the standardised mean for all three indices, and they were
also the only participants in this group with actual VIQ scores lower than 85. All seven of these participants also had
scores significantly lower than predicted on all three memory indices, supporting the above suggestion that a number
of participants were experiencing widespread difficulties.

For the 32 participants whose DKEFS scores were all higher than 1 S.D. below the standardised mean, only 2
showed lower than expected scores on all the three memory indices. However, for another 18 participants, significantly
lower than predicted scores on one (9 participants) or two (9 participants) of the memory indices was indicated. An
examination of actual scores for this group of participants indicated that 7 had scores that were lower than 85 on at
least one memory index, and this was most commonly (6 participants) in relation to the General Memory Index.

On the general ability measures, 14 of this group (N = 32) showed no evidence of decline, and only 2 scored
significantly lower than their predicted score on all three intelligence measures. Only one of these two participants had
also scored below predicted levels on all three memory indices. None of this group had actual scores for PIQ, VIQ or
FSIQ that were lower than 85.

3.4. Overview

When all data were examined together (i.e., DKEFS, WMS-III and WAIS-III), only nine participants (9.47%) showed
no evidence of impairment on any measure. No participant showed a significant difference between their actual score
and their WTAR predicted score on the WAIS-III only, but seven had done so on the WMS-III alone. The remaining
participants had various combinations of lower scores on executive function measures (across all categories), memory
measures and general cognitive ability measures, with no easily discernable pattern. However, once executive function
scores became lower than 1 S.D. below the standardised mean on a number of measures (16 participants), both memory
and overall cognitive ability also showed signs of deterioration, though not always beyond the normal range. There
is, however, some indication that a small subset of these participants may be experiencing difficulties over a range of
cognitive domains.

Together, these data also suggest that cognitive decline is somewhat related to levels of physical disability. However
MS (irrespective of physical disability) does appear to lead to cognitive deterioration with only nine participants
obtaining their predicted scores or scores close to the standardised mean. Of those who scored lower than expected,
there were no clearly discernable patterns of executive dysfunction in MS. However, once executive dysfunction
progressed beyond a certain level, memory in particular, was usually also affected.

4. Discussion

This study sought to provide a comprehensive picture of the patterns of cognitive performance in a substantial
community-based sample of participants with MS. Of particular interest was the nature and extent of executive dys-
function, as a systematic evaluation of the range of cognitive skills encompassed in that concept had not previously been
examined in any one MS sample. In association with this, an attempt was made to determine any regularly co-occurring
cognitive weaknesses in areas of memory or general ability.

Overall, the MS participants in this large sample showed little evidence of depression, and apart from some influence
on processing speed, mood did not generally affect cognitive performance. This is contrary to previous findings, which
suggest that depressive tendencies are a common accompaniment to MS (e.g., Arnett, Higginson, Voss, Bender, et al., 1999; Arnett, Higginson, Voss, Wright, et al., 1999; Dalton & Heinrichs, 2005; Landro, Sletvold, & Celius, 2000; Minden et al., 1990). However, many studies which concluded that their samples had a tendency to depression (e.g., Andrade et al., 1999) used measures such as the Beck Depression Inventory, in which all symptoms of depression are combined into the one score. In contrast, the current study illustrated the advantage of using the CMDI for this community, and similar, clinical samples, as it was able to clarify, whether the obtained depression scores were indicative of a level of depression per se or whether elevated scores were primarily the result of other disease symptoms.

Two distinct groups were evident in relation to levels of physical disability. The first exhibited only minimal physical limitations, while the other recorded more severe limitations. In general, although some relationship between cognitive deterioration and levels of physical disability was seen on measures of executive function, its level of influence was shown to be low.

4.1. General cognitive ability

Overall the general cognitive ability levels of the participants in this sample fell within the average range, but within this group there were a number of participants whose performance was significantly lower than their predicted score. Given the current levels of performance this would suggest that prior to MS the level of general ability for many in this sample would have been high. Although in a minority of cases this may have been the result of compromised motor skills, the suggestion of a high level of pre-morbid performance is supported by the Australian study (Mathias, Barrett-Woodbridge, & Bowden, 2004), which found the scores predicted by the Wechsler Test of Adult Reading to be somewhat conservative. Thus, the WTAR may have underestimated the pre-morbid IQ of our sample, strengthening the suggestion that this sample was of above average intelligence. Thus, for a number of people in this sample the recognition of declining cognitive skills would be a factor that must only add to the numerous personal frustrations that this disease brings.

The scores from the WAIS indices suggest the presence of little or no impairment in this sample. The exception to this was the Processing Speed Index. However, this score is largely influenced by the integrity of the participant’s motor skills, and in this sample possibly depressed mood, and therefore is not a completely reliable indication of the processing speed it purports to measure. Although in this sample the means of both Symbol Search and Digit Symbol Coding were below the standardised mean, the scores for Digit Symbol Coding were significantly lower than the scores for Symbol Search, suggesting that motor slowing may be the predominant reason behind the poor performance. In keeping with this, previous studies have suggested that the Digit Symbol subtest of this index is frequently one of the lowest subtests scores, and this was certainly the case here (Andrade et al., 1999). Even with this confounding issue, the mean scores for the group as a whole showed only approximately a 4-point difference between the Verbal IQ and the Performance IQ, which is considerably less than the 7–10-point differences reported in previous studies (Rao, 1996). It was evident however that the individual indices making up the Performance IQ (Perceptual Organisation and Processing Speed), and as a consequence, the aggregate Performance IQ score, did show greater variability in their scores than the other indices. In keeping with the findings of McIntosh-Michaelis et al. (1991), little evidence of deficits in Verbal IQ was revealed. Thus, deterioration in the perceptual rather than the verbal domain was more frequent in this sample.

Although direct comparisons with other studies are not possible, the characteristics of the two clusters found within this sample also support previous findings, which suggest that weaknesses are most likely to occur in those abilities that are assessed by the Performance IQ. Consistent with this, predicted scores (from the WTAR), suggested that while most participants were performing within normal limits, more than one third of this sample had experienced some decline in their intellectual functioning. Where overall achievement levels were still high, this deterioration seemed to be most often a selective decline in perceptual and performance skills rather than verbal abilities. Where overall achievement levels were lower, the decrease in performance was more likely to be across the board. These findings need to be interpreted with some caution as it is acknowledged that the prediction of PIQ from the WTAR is not as accurate as VIQ.

4.2. Memory

The group results of this sample on the Wechsler Memory Scales-III did not reveal a significant deficit in any of the indices, but performance on both immediate and delayed visual recall was significantly poorer than auditory immediate
and delayed recall. These findings differ from previous studies that report widespread memory impairments, including deficits in long term memory, visual and verbal learning, immediate and delayed recall and recognition (Fischer, 1988; Rolania et al., 2006; Ruggieri et al., 2003; Staffen et al., 2002; Thornton & Raz, 1997; Wishart & Sharpe, 1997), and no visual/auditory differential. Such discrepancies could be due to the different tests and norms used for assessment, or could be a consequence of sample differences from a very heterogeneous pool of people. However, given that a primary target for the degenerative processes of MS is the optic nerve, it is possible that some degradation of the visual stimuli occurs prior to or during the encoding process. It may therefore be useful in future studies to conduct a visual screen to clarify this issue.

In contrast to the conclusion drawn from group data that memory is not impaired, and more in line with the results of previous studies, the numbers of participants scoring lower then expected on each of the three primary indices of the Wechsler Memory Scales-III were relatively high (more than half the group on some indexes). Also, in contrast to the general ability scores, for those whose deterioration extended over all three memory indices, their actual performance levels were also low. Similar numbers showed some degree of impairment on short term (immediate) and long term memory (general) measures. Thus, there is evidence of more widespread memory impairment similar to that reported elsewhere when participants are looked at on a case-by-case basis, than when data is averaged across the group. However, this apparent deterioration in memory does need to be interpreted somewhat cautiously due to the wide prediction intervals of the WTAR for WMS-III scores. In future studies this could be overcome by the use of a matched control group.

The three cluster grouping of participants based on the WMS-III Index scores followed the pattern of previous research (Beatty et al., 1996; Fischer, 1988). That is, two clusters indicating average or above levels of performance and minimal modality differences, while the third was characterised by lower levels of performance and a pronounced modality differential. Although different assessment tools were used in the previous studies, a further common factor was that the middle cluster in all studies was made up of approximately 50% of the participants. One point of difference was the selective impairment in long term versus short term memory found in the two higher scoring clusters in the Fischer study, which was not evident in this study. This could be a result of the ‘averaging’ of greater numbers of participants in this study, or it could be a consequence of the difference between two samples taken from a very heterogeneous subset of people.

Together, these findings suggest that for those with MS, memory impairment is either selectively related to the visual modality, or visual memory is more severely compromised than auditory memory. Although there was no screening for visual impairment in this research, and some participants required corrective lenses, there was no evidence to suggest that visual impairment per se was responsible for this discrepancy. For the large majority (83%) of participants with ‘impaired’ visual memory scores (scores <85), there was no significant difference between the recall of faces and the recall of family pictures for either short term or long term recall. Where there was a difference, faces were more accurately recalled than the family pictures. The reasons behind this could be the focus of future research.

4.3. Executive functions

The majority of this sample showed evidence of below average performance on some aspects of executive functioning, which is much higher than previous reports of 15–20% impairment in samples of those with MS (Fischer, 2001; Fischer et al., 1994; Rao et al., 1991). This may be in part due to the use of the DKEFS, which permitted a much more comprehensive assessment of executive dysfunction than has previously been carried out (i.e. more categories tested). It was also the case, however, that almost two thirds of those who indicated some impairment, only presented with deficits on a few tasks, and thus may not have problems in ‘real life’ situations. Indeed, given the number of tests administered some ‘impaired’ scores were likely to be due to chance. However, 16 (17%) of our participants had lower than average scores on more than 5 measures. In terms of the types of weaknesses observed, results from this study largely concur with previous findings that suggest shifting and inhibition, along with fluency are commonly seen deficits in MS (Beatty et al., 1989, 1995; Beatty & Monson, 1996; Caltagirone et al., 1991; Vitkovitch, Bishop, Dancey, & Richards, 2002). However, as with the key shifting and inhibition measures were time related (Trails and Colour Word Interference), this raises the possibility that slowed information processing speed may have influenced performance. Furthermore, not only are several of the DKEFS tests timed, they also require a physical response, which may be slowed in MS. Thus, the number of participants showing ‘true’ executive dysfunction may be lower than the figures given above. Thus further research could attempt to separate executive dysfunction from the effects of motor slowing.
It was also evident, that there was no ‘typical’ pattern of impairment that could be associated with MS. Thus, although the DKEFS allowed a much more thorough examination of executive function in MS, the use of this measure has done little to clarify the executive dysfunctions most commonly associated with MS. Rather it provides support for the suggestion that patterns of cognitive performance in MS differ between individuals, as does the disease course. Also, studies using tests which simulate more realistic situations (e.g., Behavioural Assessment of Dysexecutive Syndrome (BADS)) may aid in clarifying the effects of any impairments on day-to-day life.

Overall, based on predicted scores and normative data, only nine participants showed no suggestion of cognitive deterioration on any of the assessments. This is an indication that it is unusual for MS to occur without some cognitive decline. Interestingly, the majority of those whose actual scores where significantly lower than predicted on more than one measure, showed weaknesses in all three areas (executive functioning, memory and general ability). Thus, those with MS are likely to experience a wide range of cognitive ‘symptoms’ which are not focused on one particular aspect of functioning. In total, approximately 16% of participants in this study suggested extensive deterioration in cognitive ability. Thus, not only do these people have to contend with the physical problems associated with MS, but also some may have difficulties in relation to planning, organising, problem solving and remembering day-to-day tasks.

This study also highlights the need for detailed analysis of individual cases rather than relying on group data if a realistic picture of the nature and extent of impairment is to be obtained. This is especially true with a clinical group such as those with Multiple Sclerosis whose impairment patterns are known to be extremely heterogeneous.

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References


