The Norwegian translation of the brief international cognitive assessment for multiple sclerosis (BICAMS)

Ellen Skorve[a,b,*], Astri J. Lundervold[c], Øivind Torkildsen[a,b], Kjell-Morten Myhr[a,b]

[a] Norwegian Multiple Sclerosis Competence Center, Department of Neurology, Haukeland University Hospital, Bergen, Norway
[b] Department of Clinical Medicine, University of Bergen, Bergen, Norway
[c] Department of Biological and Medical Psychology, University of Bergen, Bergen, Norway

ARTICLE INFO

ABSTRACT

Background: Cognitive impairment is a common symptom in all stages of multiple sclerosis (MS), yet it is underreported and not routinely evaluated. The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) is a short and easily administered test battery for screening of cognitive impairment in MS that can be completed within 15 min and incorporated into routine clinical practice. The test battery consists of the oral version of the Symbols Digit Modalities Test (SDMT) and the initial learning trials of the California Verbal Learning Test 2nd edition (CVLT-II) and the Brief Visuospatial Memory Test Revised (BVMT-R).
Objective: To investigate if the Norwegian version of the BICAMS could identify cognitive impairment in early stages of MS and be used as part of routine follow-up procedures.
Methods: A total of 65 relapsing-remitting MS (RRMS) patients and 68 healthy controls were examined with the BICAMS test battery. A randomly selected subset of 29 controls were retested 1–4 weeks after baseline. All participants were screened for anxiety and depression using the Hospital Anxiety and Depression Scale (HADS).
Results: There were statistically significant differences between the patients with MS and the healthy controls on all three subtests, and the differences remained significant for the CVLT-II ($p = 0.003$) and BVMT-R ($p = 0.011$) after adjusting for education. There were no statistically significant correlations between BICAMS scores and anxiety and depression. SDMT and BVMT-R results in the control group at baseline and re-test were strongly correlated ($r \geq 0.70$, $p < 0.001$), and CVLT-II achieved an adequate value of $r = 0.60$ ($p = 0.001$). On the SDMT, there was a statistically significant improvement between the two test-sessions. Cognitive impairment, defined as an abnormal test score on ≥ 1 subtest, was identified in 46.2% of the patient sample, whereas 15.4% were considered cognitively impaired on ≥ 2 subtests.
Conclusion: This study supports that the Norwegian version of the BICAMS should be included as a screening procedure for cognitive impairment in Norwegian MS patients.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system, affecting approximately 2.3 million people worldwide (Thompson et al., 2018). Cognitive impairment is a well-documented symptom in MS, and affects up to 65% of the patients (Amato et al., 2006; Bobholz and Rao, 2003; Chiaravalloti and DeLuca, 2008; Rao et al., 1991). It is present in all subtypes and at all stages of the disease, and it is known to progress over time (Amato et al., 2001, 2006; Patti et al., 2009; Rao et al., 1991). Many patients with MS exhibit signs of cognitive impairment even before the first physical symptom of the disease manifests (Cortese et al., 2016), which implies a preclinical disease activity affecting cognition. The high prevalence rate, along with the evidence of preclinical cognitive symptoms, highlight the need for a standardized tool for screening of cognitive function in patients with MS.

Awareness of cognitive symptoms associated with MS has improved during the recent years. Traditionally, the cognitive assessment of patients with MS has been performed by trained neuropsychologists in specialized centers, and involves time-consuming comprehensive test batteries, such as the Brief Repeatable Battery of Neuropsychological tests (BRB-N) and the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS) (Benedict et al., 2006; Strober et al., 2009). Such evaluations have been reserved for patients who already have an apparent degree of cognitive impairment, and is not routinely offered to young or employed patients with MS. In order to detect the

early, subtle changes in cognition, there has been a call for a short, sensitive and easily administered test battery; one that can be incorporated into standard routines when diagnosing and following up patients with MS. The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) was developed for this purpose (Langdon et al., 2012).

The BICAMS can be completed in 15 min without requiring any special equipment or extensive assessor training, and is shown to be sensitive to cognitive changes associated with MS (Langdon et al., 2012). Subtests are included based on psychometric qualities (reliability, validity and sensitivity) and international applicability and feasibility. The BICAMS evaluates (1) information processing speed by the Symbol Digit Modalities Test (SDMT), (2) verbal memory function by the learning trials of the California Verbal Learning test, 2nd edition (CVLT-II) and (3) visual memory function by the learning trials of the revised Brief Visuospatial Memory Test (BVMT-R) (Langdon et al., 2012). The test battery thereby includes measures of the cognitive functions that are most commonly affected in MS (Chiaravalloti and DeLuca, 2008; Langdon, 2011). An international standard for validation has been developed (Benedict et al., 2012) and the BICAMS has been translated and validated in several countries (Corfield and Langdon, 2018; Costers et al., 2017; Dusankova et al., 2012; Filser et al., 2018; O'Connell et al., 2015; Polychroniadou et al., 2016; Sandi et al., 2015; Sousa et al., 2018; Walker et al., 2016).

This paper presents results on the Norwegian version of the BICAMS in a cohort of newly diagnosed MS patients with disease duration of less than 6 years. From previous studies we expected that the tests would discriminate well between the patients and the controls and that a significant proportion of the MS patients would be defined as impaired on at least one of the tests. The BICAMS tests were used in accordance with the proposed international validation protocol (Benedict et al., 2012).

2. Methods

2.1. Study population

2.1.1. Patients

All relapsing-remitting MS (RRMS) patients between 18 and 65 years of age, with first-time diagnosis (Polman et al., 2011) between January 1st 2014 and September 1st 2017, were screened using hospital records at Haukeland University Hospital, Western Norway. A total of 158 patients with less than three years of documented disease activity prior to diagnosis were invited to participate in the study, and 98 (62%) agreed to participate. Following a telephone interview, 33 patients were excluded, leaving 65 RRMS patients for inclusion. Reasons for exclusion were: self-reported MS-related symptoms more than three years prior to diagnosis ($n = 18$), primary language not Norwegian ($n = 1$), neurological or psychiatric comorbidities that could impede cognition ($n = 2$), affiliation to other health care region ($n = 1$), unresponsive to contact ($n = 1$), withdrawal of consent ($n = 2$), clinically isolated syndrome or progressive subtype ($n = 8$).

2.1.2. Controls

We recruited 68 healthy controls from the community through posters in the Hospital buildings and advertisements on the Norwegian MS Society web site. The controls were between 18 and 65 years of age with Norwegian as their primary language. None of the participants reported present or previous neurological or psychiatric illnesses that could impede cognition.

2.2. Procedures

The study was approved by the Regional Ethics Committee of Western Norway (registration number 2016/31/REK Vest), and participation was based on written informed consent.

The controls received two cinema tickets and free parking as compensation for their participation, and the patients with MS were compensated for their deductible related to the study examinations.

2.2.1. Questionnaires

To assess whether depression or anxiety influenced cognitive performance, both the patients with MS and the healthy controls were asked to complete the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) which has been translated into Norwegian and validated for use in the MS population (Pais-Ribeiro et al., 2018). In addition, all participants completed a self-report questionnaire listing their education, employment status and general health status.

2.2.2. Physical examination

All patients with MS were examined with a full neurological evaluation, including scoring of the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983).

2.2.3. Neuropsychological tests: BICAMS

The oral version of the Symbol Digit Modalities Test (SDMT) (Smith, 1982) is included as a measure of information processing speed. An A4 sheet of paper with rows of nine abstract symbols arranged pseudo-randomly is presented to the subject. A cipher key linking each of these symbols to a single digit is located at the top of the page. After a short written practice session on the first 10 symbols, the test subject has to voice the digit corresponding to each symbol as rapidly as possible for 90 s. The outcome measure is the number of correctly identified symbols in the 90-second timeframe. No translation is required as the symbols have no semantic meaning. A previous study has reported high sensitivity, a good test-retest reliability and only a minor learning effect on this version of the SDMT (Strober et al., 2009). The same version of SDMT was therefore presented in the test and re-test session.

The first five learning trials of the official Norwegian translation (Lundervold, 2004) of the 2nd edition of the California Verbal Learning Test (CVLT-II) (Delis et al., 1987) are included to obtain a measure of verbal memory function. The restriction to the learning trials is based on results from previous studies (Stegen et al., 2010). The examiner reads aloud a list of 16 words (List A) and the test subject is then asked to repeat as many words as possible. The list is repeated five times, and the number of correct words remembered across the five trials is used as the outcome measure. To reduce the risk of a learning effect, an alternate list of 16 words is included in the re-test session. The use of such an alternate form is highly recommended during the short-interval repeated assessment of memory function in patients with MS (Benedict, 2005), but studies validating alternate forms of the shortened version of CVLT-II included in the BICAMS are still missing. For the re-test session in the present study, the 16 words from the interference list of the standard format of CVLT-II (List B) were selected, as they were not presented as part of the first test session and is constructed similarly to the original list.

The first three learning trials of the BVMT-R (Benedict, 1997) are included to obtain a measure of visual memory function. The restriction to the learning trials is based results from previous studies (Benedict et al., 2006; Costers et al., 2017). A stimulus sheet showing an array of 2×3 abstract designs is presented to the test subject for 10 s. When the stimulus is then hidden from view, the test subject is asked to draw from memory the same abstract designs in the same spatial arrangement as presented on the stimulus sheet. This is repeated three times and the outcome measure is the total score achieved over all three trials. There is a potential learning effect with repeated testing. The test stimuli are therefore different at baseline and re-test (Form 1 and Form 2, respectively).

2.3. Statistical analyses

Statistical analyses were performed using SPSS version 24 (IBM

Corp., Armonk, NY), and figures were made using StataSE version 15 (StataCorp LLC, College Station, Texas). Statistical significance was set at alpha level < 0.05. Between-group differences were examined with student's t-test and chi-square for continuous and categorical variables, respectively. Effect sizes were calculated according to Cohen's d statistic (0.2 = small, 0.5 = medium, 0.8 = large). The relationship between the BICAMS scores and anxiety/depression (HADS-scores) was calculated by running a Pearson's correlational analysis. Correlation analysis was also used to assess the test-retest reliability of the BICAMS subtests and paired t tests were calculated to evaluate improvement from baseline to re-test in the control group. Cut-off values were calculated for each subtest (≤ 1.5 standard deviations below the mean of the control group), and participants were defined as cognitively impaired or cognitively preserved based on the occurrence of abnormal test scores on one, two and three subtests, respectively. A stepwise linear regression was performed to assess if BICAMS performance predicted self-reported employment status. Age, gender, education level, EDSS, disease duration and HADS-scores were entered as predictors on the first step and the BICAMS-scores on the second step.

3. Results

3.1. Demographic characteristics

We included 65 patients with RRMS and 68 healthy controls in the study. Baseline demographic characteristics are outlined in Table 1. There were no statistically significant differences between the groups regarding age or gender, but the number of participants with the lowest level of education was significantly higher in the MS than the control group, with a corresponding higher number of controls at the two highest levels. Almost all participants in both groups were employed, and more than two thirds were employed full time

All participants in the MS group had a relapsing-remitting subtype, with an EDSS score ranging from 0 to 3 (mean 1.28 ± 0.88) and an average disease duration (time from first documented clinical symptom to BICAMS testing) ranging from 0.25 to 5.33 (mean 1.81 ± 1.23) years.

3.2. Impact of anxiety and depression on BICAMS performance

The scores on the Hospital Anxiety and Depression Scale (HADS) showed that the patients with MS reported significantly higher levels of anxiety compared to the controls (Table 2), with a non-significant difference in level of depression. The combined anxiety and depression score (HADS-total) was significantly higher in the MS than the control group ($p = 0.041$). The level of anxiety and depression did not, however, correlate significantly to the BICAMS scores in either group (Table 3).

Table 1
Baseline demographic characteristics in the MS group (MS) and the healthy control group (HC).

	MS (N = 65)	HC (N = 68)	p-value
Gender male/female, N (% female)	23/42 (64.6)	23/45 (66.2)	0.850
Age (years), mean ± SD	37.02 ± 10.40	38.13 ± 11.40	0.556
Education, N			
< 14 years	23	11	*0.038*
14–16 years	24	31	
> 16 years	18	26	
Employed,%	89.2	97.0	0.080
Fulltime,%	70.3	76.6	0.423
Disease duration (years), mean ± SD			
Since first symptom	1.81 ± 1.23	–	–
Since diagnosis	1.08 ± 0.74	–	–
EDSS, mean ± SD	1.28 ± 0.88	–	–

SD = Standard deviation. EDSS = Expanded Disability Status Scale.

Table 2
Group differences on measures of anxiety and depression among patients with MS and healthy controls (HC).

	MS Mean (± SD)	HC Mean (± SD)	t	p-value
HADS-Anxiety	5.64 (± 4.00)	4.29 (± 3.16)	2.145	0.034
HADS-Depression	2.95 (± 3.23)	2.20 (± 2.48)	1.494	0.138
HADS-Total	8.59 (± 6.49)	6.48 (± 5.11)	2.062	0.041

SD = Standard deviation. HADS = Hospital Anxiety and Depression Scale.

Table 3
Correlations between the BICAMS subtests and anxiety/depression.

Test	Group	HADS-total	
		Pearson's r	p-value
SDMT	*MS*	− 0.018	0.888
	HC	− 0.034	0.787
CVLT-II	*MS*	− 0.135	0.288
	HC	0.024	0.846
BVMT-R	*MS*	− 0.080	0.532
	HC	0.006	0.962

MS = (patients with) Multiple Sclerosis. HC = Healthy controls. HADS = Hospital Anxiety and Depression Scale. **SDMT =** Symbols Digit Modalities Test. **CVLT-II =** California Verbal Learning Test, 2nd edition. **BVMT-R =** Brief Visuospatial Memory Test, Revised.

3.3. Group differences on BICAMS measures

The mean scores on the SDMT, CVLT-II and BVMT-R were all significantly lower in the MS group than in the control group (Table 4), with differences of small to medium effect sizes. When adjusting for group mismatch in education and anxiety/depression, the scores remained significantly lower in the MS group on the CVLT-II and the BVMT-R, but not for the SDMT.

3.4. Test-retest data in the control group

We retested the healthy controls 7 to 32 (mean 19.63 ± 7.87) days after the baseline assessment and the test-retest data are shown in Table 5 and Fig. 1. Strong correlations between the results at baseline and retest were found for all subtests; the SDMT and BVMT-R both achieved excellent r-values of ~ 0.80 ($p < 0.001$) whereas the CVLT-II obtained an r-value of ~ 0.60 ($p = 0.001$). There was a statistically significant improvement on the SDMT between the two sessions (~ 3.5 points, $p = 0.024$).

3.5. Cognitive impairment in the MS group

A score ≤ 1.5 standard deviations below the mean score of the control group defined the cut-off value for cognitive impairment on each of the three BICAMS tests. Following the criteria of ≥ 1 abnormal test score (Dusankova et al., 2012), 46.2% of the patient sample were considered cognitively impaired (Table 6). They were most likely to be impaired on the CVLT-II, with 30.8% of the patients scoring below the cut-off value. On the BVMT-R and SDMT, 26.2% and 10.8% were considered cognitively impaired, respectively. When the definition of cognitive impairment was defined as ≥ 2 abnormal tests, only 15.4% of the patients with MS were considered cognitively impaired, and a small subset of 6.2% scored below the cut-off value on all three tests.

3.6. BICAMS and employment

There was no significant difference between the groups in regards to overall employment status (Table 1). When entered into a stepwise regression model, only age ($F = 5.077$, $p = 0.028$) was retained in the

Table 4
Group differences on BICAMS measures, independent samples t-test.

Test	MS (mean ± SD)	HC (mean ± SD)	Mean Δ	t	p-value	Adjusted p-value*	Cohen's d
SDMT	54.65 ± 10.79	58.52 ± 10.53	3.87	−2.09	0.039	0.201	0.37
CVLT-II	54.55 ± 10.86	60.32 ± 7.75	5.77	−3.51	0.001	0.008	0.62
BVMT-R	26.55 ± 5.76	29.03 ± 4.01	2.48	−2.89	0.005	0.027	0.51

HC = Healthy controls. Δ = difference. **SD** = Standard deviation. **SDMT** = Symbols Digit Modalities Test. **CVLT-II** = California Verbal Learning Test, 2nd edition.
BVMT-R = Brief Visuospatial Memory Test, Revised.
  * Adjusted for level of education and anxiety/depression.

model as a significant predictor (variables entered: age, gender, disease duration (from onset and from diagnosis), level of education, EDSS, HADS-scores and raw scores on the BICAMS subtests).

4. Discussion

The present study found that the BICAMS subtests discriminated well between the MS and the control group, a finding that was retained for CVLT-II and BMVT-R when accounting for level of education and anxiety/depression. Almost half of the MS patients were identified with cognitive impairment on at least one subtest, and results at baseline and re-test were significantly correlated on all BICAMS tests in the control group, with a weak improvement on the SDMT.

Most other published BICAMS-studies present data from patient groups with mean disease duration of ∼10 years (Corfield and Langdon, 2018). To our knowledge, this is the first BICAMS-study to investigate newly diagnosed patients with a specific criterion of less than three years from first clinical symptom to diagnosis. This provides an insight into the development of cognitive impairment in the earliest stages of the disease, but may also limit the value of direct comparisons to other BICAMS-studies.

With cognitive impairment defined as at least one abnormal test score (Dusankova et al., 2012), the BICAMS battery identified 46.2% of the current patient sample as cognitively impaired. This is lower than the prevalence found in Canada (57.9%) (Walker et al., 2016), Ireland (57%) (O'Connell et al., 2015) and Hungary (52.3%) (Sandi et al., 2015), which were all in line with the prevalence documented by the Czech study comparing BICAMS and MACFIMS (55% and 58% respectively) (Dusankova et al., 2012). It was, however, significantly higher than the prevalence reported from the Portuguese (24.8%) (Sousa et al., 2018) and German (32.6%) (Filser et al., 2018) studies. When cognitive impairment was defined as at least two abnormal test scores, the number of patients with impairment was cut to a third of the original estimate (15.4%), indicating that the cognitive impairment should be characterized as mild in most of the affected patients.

Separate analyses of the subtests showed, in contrast to other BICAMS-publications, that CVLT-II identified impairment in a higher number of patients (30.8%) than the other subtests (BVMT-R 26.4% and SDMT 10.8%) (Costers et al., 2017; Filser et al., 2018; Polychroniadou et al., 2016; Sandi et al., 2015; Sousa et al., 2018; Walker et al., 2016). The low rate of impaired SDMT scores was surprising especially since low scores on this subtest has been reported to be a strong indicator of cognitive impairment in patients with MS

(Benedict et al., 2017). The non-significant proportion of patients identified as impaired by the SDMT in our sample may be explained by the inclusion of only RRMS patients in an early stage of the disease.

The SDMT showed a statistically significant improvement from baseline to retest at a group-level, suggesting that at least some of the participants may have remembered symbol-number associations over the short time-period between the two test sessions. However, the lack of significant correlations between test intervals and SDMT score change in the present study did not support this (data not shown). In any case, such a learning effect will probably be milder with the longer time-frame planned for the re-test of MS patients (≥ 12 months). For the CVLT-II and BVMT-R we found non-significant differences between performances at the two time points and significant correlations between performances a baseline and re-test. Although results for the alternate word lists in CVLT-II fell short of the requested goal from the validation standards of $r \geq 0.70$ (Benedict et al., 2012), we conclude that our results support the use of all three tests as part of follow-up procedures in Norwegian MS patients. However, the validity of the re-test list for the CVLT-II included in the present study should be further investigated.

Despite the relatively high prevalence of cognitive impairment in this sample, there was a low degree of unemployment (10.8%) and only age was found to be a statistically significant predictor of employment status at this early stage of the disease. This indicates that most patients continue to work in spite of mild signs of cognitive impairment. With early identification of cognitive impairment we may optimize treatment, implement coping strategies and work place customization, as well as cognitive rehabilitation (Goverover et al., 2018; Hamalainen and Rosti-Otajarvi, 2016), and therefore hopefully postpone or prevent early retirement due to MS. Exactly how to define a "positive" screening result on the BICAMS in clinical practice, however, remains unclear. Using the one-or-more criterion as a threshold for referral to further evaluation may overload the local neuropsychological services and classify normal variation as pathology. Restriction to the two-or-more criterion may, on the other hand, overlook patients in real need of help, with the risk of giving treatment options too late to be effective. Further investigation into the optimal scoring and follow-up of a positive screening result on the BICAMS is therefore required.

5. Conclusions

Used in accordance with the proposed international validation protocol (Benedict et al., 2012), the Norwegian version of the BICAMS
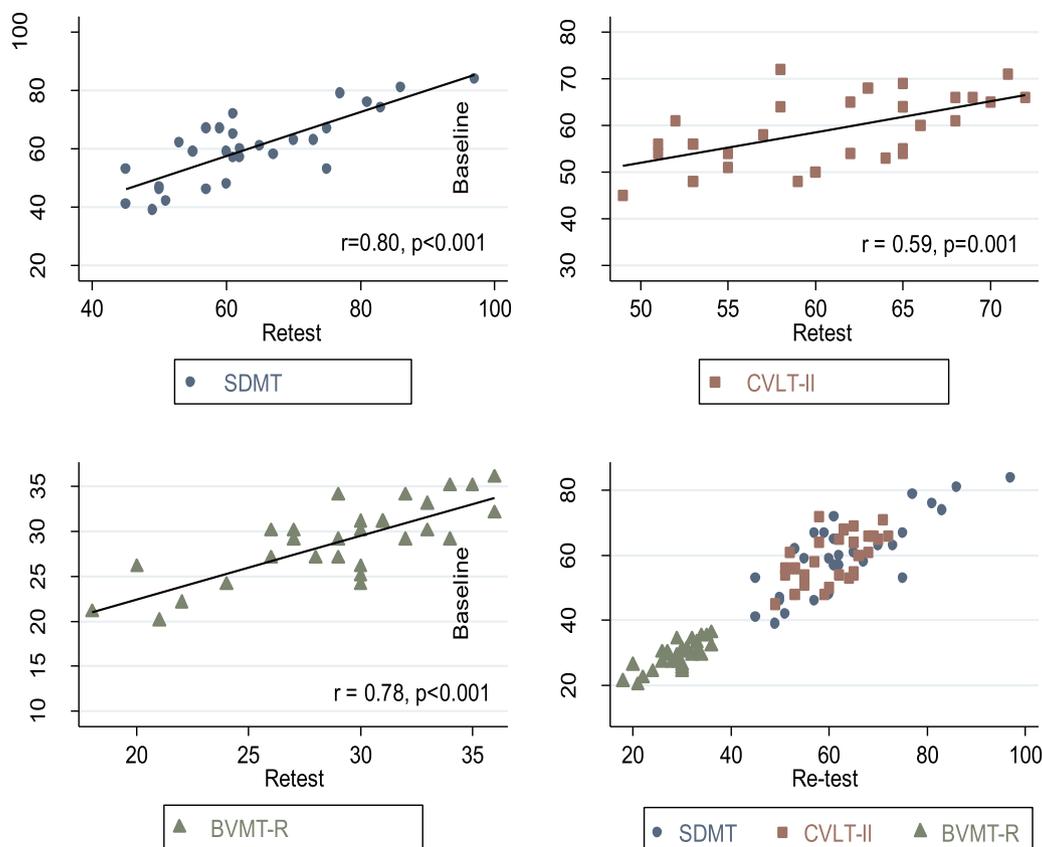
Table 5
Test-retest means and correlations for control group.

| | Paired samples t-test | | | | | Pearson's correlation | |
	Test Mean ± SD	Retest Mean ± SD	Mean Δ	t	p-value	Pearson's r	p-value
SDMT	60.21 ± 12.13	63.69 ± 12.90	−3.48	−2.378	0.024	0.803	< 0.001
CVLT-II	59.24 ± 7.44	61.07 ± 6.68	−1.83	−1.532	0.137	0.590	0.001
BVMT-R	28.86 ± 4.23	29.07 ± 4.68	−0.21	−0.375	0.710	0.783	< 0.001

SD = Standard deviation. SDMT = Symbols Digit Modalities Test. CVLT-II = California Verbal Learning Test, 2nd edition. BVMT-R = Brief Visuospatial Memory Test, Revised.

Fig. 1. Scatterplots and test-retest correlation data for SDMT, CVLT-II and BVMT-R in the control group.

Table 6
Estimation of cognitive impairment in the MS group.

	Cutoff-value (≤ 1.5 SD)	**MS-group**	
		N	%
Abnormal test score on SDMT	≤ *43*	7	10.8
Abnormal test score on CVLT-II	≤ *49*	20	30.8*
Abnormal test score on BVMT-R	≤ *23*	17	26.2*
≥ 1 abnormal test scores		30	46.2*
≥ 2 abnormal test scores		10	15.4*
3 abnormal test scores		4	6.2
No abnormal test scores		35	53.8*
Abnormal SDMT *and* CVLT-II		5	7.7
Abnormal SDMT *and* BVMT-R		5	7.7
Abnormal CVLT-II *and* BVMT-R		8	12.3*

SDMT = Symbols Digit Modalities Test. CVLT-II = California Verbal Learning Test, 2nd edition. BVMT-*R* = Brief Visuospatial Memory Test, Revised.
  * Pearson's Chi-square $p < 0.05$.

was found to discriminate well between MS patients and controls and identify individuals with suspect cognitive impairment in an early stage of the disease. We therefore recommend implementation of the BICAMS into clinical practice and routine evaluation of Norwegian MS patients.

CRediT authorship contribution statement

Ellen Skorve: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing - original draft, Writing - review & editing. **Astri J. Lundervold:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing - review & editing. **Øivind Torkildsen:** Data curation, Formal analysis, Methodology, Supervision, Validation, Visualization, Writing - review & editing. **Kjell-Morten Myhr:** Conceptualization, Data curation, Funding acquisition, Methodology, Resources, Supervision, Writing - review & editing.

References

Amato, M.P., Ponziani, G., Siracusa, G., Sorbi, S., 2001. Cognitive dysfunction in early-onset multiple sclerosis: a reappraisal after 10 years. Arch. Neurol. 58 (10), 1602–1606.

Amato, M.P., Zipoli, V., Portaccio, E., 2006. Multiple sclerosis-related cognitive changes: a review of cross-sectional and longitudinal studies. J. Neurol. Sci. 245 (1–2), 41–46.

Benedict, R.H., 2005. Effects of using same- versus alternate-form memory tests during short-interval repeated assessments in multiple sclerosis. J. Int. Neuropsychol. Soc. 11 (6), 727–736.

Benedict, R.H., Amato, M.P., Boringa, J., Brochet, B., Foley, F., Fredrikson, S., Hamalainen, P., Hartung, H., Krupp, L., Penner, I., Reder, A.T., Langdon, D., 2012. Brief international cognitive assessment for ms (BICAMS): international standards for validation. BMC Neurol. 12, 55.

Benedict, R.H., Cookfair, D., Gavett, R., Gunther, M., Munschauer, F., Garg, N., Weinstock-Guttman, B., 2006. Validity of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS). J. Int. Neuropsychol. Soc. 12 (4), 549–558.

Benedict, R.H., DeLuca, J., Phillips, G., LaRocca, N., Hudson, L.D., Rudick, R., Multiple Sclerosis Outcome Assessments, C, 2017. Validity of the symbol digit modalities test as a cognition performance outcome measure for multiple sclerosis. Mult. Scler. 23 (5), 721–733.

Benedict, R.H.B., 1997. Brief Visuospatial Memory Test - Revised: Professional Manual. Psychological Assessment Resources, Odessa, Florida.

Bobholz, J.A., Rao, S.M., 2003. Cognitive dysfunction in multiple sclerosis: a review of

recent developments. Curr. Opin. Neurol. 16 (3), 283–288.

Chiaravalloti, N.D., DeLuca, J., 2008. Cognitive impairment in multiple sclerosis. Lancet Neurol. 7 (12), 1139–1151.

Corfield, F., Langdon, D., 2018. A systematic review and meta-analysis of the brief cognitive assessment for multiple sclerosis (BICAMS). Neurol. Ther. 7 (2), 287–306.

Cortese, M., Riise, T., Bjornevik, K., Bhan, A., Farbu, E., Grytten, N., Hogenesch, I., Midgard, R., Smith, S.C., Telstad, W., Ascherio, A., Myhr, K.M., 2016. Preclinical disease activity in multiple sclerosis: a prospective study of cognitive performance prior to first symptom. Ann. Neurol. 80 (4), 616–624.

Costers, L., Gielen, J., Eelen, P.L., Schependom, J.V., Laton, J., Remoortel, A.V., Vanzeir, E., Wijmeersch, B.V., Seeldrayers, P., Haelewyck, M.C., D'Haeseleer, M., D'Hooghe, M.B., Langdon, D., Nagels, G., 2017. Does including the full CVLT-ii and BVMT-r improve BICAMS? evidence from a Belgian (Dutch) validation study. Mult. Scler. Relat. Disord. 18, 33–40.

Delis, D.C., Kramer, J.H., Kaplan, E., Ober, B.A., 1987. California Verbal Learning Test: Adult version Manual. The Psychological Corporation, San Antonio, Texas.

Dusankova, J.B., Kalincik, T., Havrdova, E., Benedict, R.H., 2012. Cross cultural validation of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS) and the brief international cognitive assessment for multiple sclerosis (BICAMS). Clin. Neuropsychol. 26 (7), 1186–1200.

Filser, M., Schreiber, H., Pottgen, J., Ullrich, S., Lang, M., Penner, I.K., 2018. The brief international cognitive assessment in multiple sclerosis (BICAMS): results from the german validation study. J. Neurol. 265 (11), 2587–2593.

Goverover, Y., Chiaravalloti, N.D., O'Brien, A.R., DeLuca, J., 2018. Evidenced-Based cognitive rehabilitation for persons with multiple sclerosis: an updated review of the literature from 2007 to 2016. Arch. Phys. Med. Rehabil. 99 (2), 390–407.

Hamalainen, P., Rosti-Otajarvi, E., 2016. Cognitive impairment in MS: rehabilitation approaches. Acta Neurol. Scand. 134 Suppl. 200, 8–13.

Kurtzke, J.F., 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 33 (11), 1444–1452.

Langdon, D.W., 2011. Cognition in multiple sclerosis. Curr. Opin. Neurol. 24 (3), 244–249.

Langdon, D.W., Amato, M.P., Boringa, J., Brochet, B., Foley, F., Fredrikson, S., Hamalainen, P., Hartung, H.P., Krupp, L., Penner, I.K., Reder, A.T., Benedict, R.H., 2012. Recommendations for a brief international cognitive assessment for multiple sclerosis (BICAMS). Mult. Scler. 18 (6), 891–898.

Lundervold, A.J., Sundet, K.S., 2004. Norsk Versjon Av CVLT-II. Manualsupplement. Psykologiforlaget AB, Oslo.

O'Connell, K., Langdon, D., Tubridy, N., Hutchinson, M., McGuigan, C., 2015. A preliminary validation of the brief international cognitive assessment for multiple sclerosis (BICAMS) tool in an irish population with multiple sclerosis (MS). Mult. Scler. Relat. Disord. 4 (6), 521–525.

Pais-Ribeiro, J.L., Martins da Silva, A., Vilhena, E., Moreira, I., Santos, E., Mendonca, D., 2018. The hospital anxiety and depression scale, in patients with multiple sclerosis. Neuropsychiatr. Dis. Treat. 14, 3193–3197.

Patti, F., Amato, M.P., Trojano, M., Bastianello, S., Tola, M.R., Goretti, B., Caniatti, L., Di

Monte, E., Ferrazza, P., Brescia Morra, V., Lo Fermo, S., Picconi, O., Luccichenti, G., Group, C.S., 2009. Cognitive impairment and its relation with disease measures in mildly disabled patients with relapsing-remitting multiple sclerosis: baseline results from the cognitive impairment in multiple sclerosis (COGIMUS) study. Mult. Scler. 15 (7), 779–788.

Polman, C.H., Reingold, S.C., Banwell, B., Clanet, M., Cohen, J.A., Filippi, M., Fujihara, K., Havrdova, E., Hutchinson, M., Kappos, L., Lublin, F.D., Montalban, X., O'Connor, P., Sandberg-Wollheim, M., Thompson, A.J., Waubant, E., Weinshenker, B., Wolinsky, J.S., 2011. Diagnostic criteria for multiple sclerosis: 2010 revisions to the mcdonald criteria. Ann. Neurol. 69 (2), 292–302.

Polychroniadou, E., Bakirtzis, C., Langdon, D., Lagoudaki, R., Kesidou, E., Theotokis, P., Tsalikakis, D., Poulatsidou, K., Kyriazis, O., Boziki, M., Papadopoulos, G., Boura, E., Sintila, L., Hatzigeorgiou, S., Ziamos, C., Ioannidis, P., Karacostas, D., Grigoriadis, N., 2016. Validation of the brief international cognitive assessment for multiple sclerosis (BICAMS) in greek population with multiple sclerosis. Mult. Scler. Relat. Disord. 9, 68–72.

Rao, S.M., Leo, G.J., Bernardin, L., Unverzagt, F., 1991. Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. Neurology 41 (5), 685–691.

Regional Ethical Comittee. (2016/31/REK Vest) Approved in 2016, case number 31, REK Vest = Regional Ethics Comittee of Western Norway.

Sandi, D., Rudisch, T., Fuvesi, J., Fricska-Nagy, Z., Huszka, H., Biernacki, T., Langdon, D.W., Langane, E., Vecsei, L., Bencsik, K., 2015. The hungarian validation of the brief international cognitive assessment for multiple sclerosis (BICAMS) battery and the correlation of cognitive impairment with fatigue and quality of life. Mult. Scler. Relat. Disord. 4 (6), 499–504.

Smith, A., 1982. Symbol Digit Modalities Test: Manual. Western Psychological Services, Los Angeles.

Sousa, C., Rigueiro-Neves, M., Miranda, T., Alegria, P., Vale, J., Passos, A.M., Langdon, D., Sa, M.J., 2018. Validation of the brief international cognitive assessment for multiple sclerosis (BICAMS) in the Portuguese population with multiple sclerosis. BMC Neurol. 18 (1), 172.

Stegen, S., Stepanov, I., Cookfair, D., Schwartz, E., Hojnacki, D., Weinstock-Guttman, B., Benedict, R.H., 2010. Validity of the california verbal learning test-ii in multiple sclerosis. Clin. Neuropsychol. 24 (2), 189–202.

Strober, L., Englert, J., Munschauer, F., Weinstock-Guttman, B., Rao, S., Benedict, R.H., 2009. Sensitivity of conventional memory tests in multiple sclerosis: comparing the rao brief repeatable neuropsychological battery and the minimal assessment of cognitive function in MS. Mult. Scler. 15 (9), 1077–1084.

Thompson, A.J., Baranzini, S.E., Geurts, J., Hemmer, B., Ciccarelli, O., 2018. Multiple sclerosis. Lancet 391 (10130), 1622–1636.

Walker, L.A., Osman, L., Berard, J.A., Rees, L.M., Freedman, M.S., MacLean, H., Cousineau, D., 2016. Brief international cognitive assessment for multiple sclerosis (BICAMS): canadian contribution to the international validation project. J. Neurol. Sci. 362, 147–152.

Zigmond, A.S., Snaith, R.P., 1983. The hospital anxiety and depression scale. Acta Psychiatr. Scand. 67 (6), 361–370.