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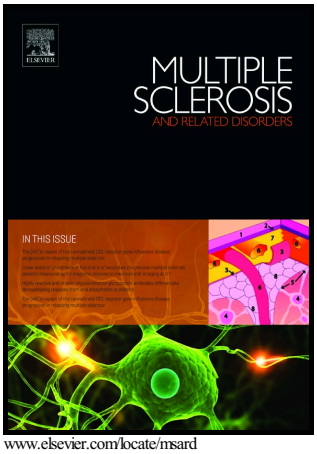

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Does including the full CVLT-II and BVMT-R improve BICAMS?
Evidence from a Belgian (Dutch) validation study

Lars Costers[1,2], Jeroen Gielen[1], Piet L. Eelen[3], Jeroen Van Schependom[1,4], Jorne Laton[1], Ann Van Remoortel[3], Ellen Vanzeir[5], Bart Van Wijmeersch[5,6], Pierrette Seeldrayers[7], Marie-Claire Haelewyck[2], Miguel D'Haeseleer[1,3], Marie-Beatrice D'hooghe[1,3], Dawn Langdon[8], Guy Nagels[1,2,3]

[1]Center for Neurosciences, Vrije Universiteit Brussel, Belgium
[2]Faculté de Psychologie et des Sciences de l'Education, Université de Mons, Belgium
[3]National MS Center Melsbroek, Belgium
[4]Radiology, UZ Brussel, Vrije Universiteit Brussel
[5]Revalidatie & MS Centrum Overpelt, Belgium
[6]Biomedisch Onderzoeksinstituut, Universiteit Hasselt, Belgium
[7]Centre Hospitalier Universitaire Charleroi, Belgium
[8]Royal Holloway, University of London, United Kingdom

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ABSTRACT

Background

The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) is a fast, easy-to-administer and already widely validated neuropsychological battery for cognition in multiple sclerosis.

Objective

The goals of our study were to validate the BICAMS in a Belgian Dutch-speaking population and to investigate to what extent including extensive versions of two of the three BICAMS subtests improved its psychometric qualities.

Methods

Ninety-seven persons with MS and ninety-seven healthy controls were included and group-matched on age, education level and gender. All participants performed the BICAMS with an extensive version of the CVLT-II and BVMT-R.

Results

The SDMT and BVMT-R were able to dissociate between the MS and healthy control group, while the CVLT-II was not. Distributions of CVLT-II scores suggest learning effects in the MS group, indicating the need for alternative word lists or the construction of an adapted version fitted for repeated administration. Including the full CVLT-II and BVMT-R did not markedly improve the psychometric qualities of the BICAMS.

Conclusion

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This study validates the BICAMS in a Belgian Dutch-speaking population and facilitates the use of it in clinical practice, while providing evidence that including full versions of the CVLT-II and BVMT-R does not increase its psychometric qualities markedly.

Keywords
Multiple sclerosis; cognition; BICAMS.

1. Introduction

Multiple sclerosis (MS) is a disease characterized by inflammatory demyelination and neurodegeneration causing a wide range of physical and cognitive problems. Cognitive impairment (CI) is very common in MS, with prevalence rates ranging from 43% to 70% (Peyser et al., 1990; Rao et al., 1991). Particularly information processing speed (Van Schependom et al., 2014), working memory (D'Esposito et al., 1996), attention and visuospatial abilities (Chiaravalloti and DeLuca, 2008) have been shown to be affected in persons with MS (PwMS). These cognitive problems have a detrimental effect on the employment status, social and vocational activities, and mental health of PwMS.

Currently, the most commonly applied neuropsychological test batteries are the Brief Repeatable Battery of Neuropsychological tests (BRB-N) (Rao et al., 1991) and the Minimal Assessment of Cognitive Function in MS (MACFIMS) (Benedict et al., 2002), which have shown great sensitivity (e.g. Strober et al., 2009). However, these test-batteries are time-demanding (45 and 90 minutes respectively), require a trained neuropsychologist and may be confounded by possible practice effects, making them unsuited for everyday practice.

To address this issue, the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) (Benedict et al., 2012; Langdon et al., 2012) was designed. Consisting of three tests, carefully selected based on psychometric properties and ease of administration, the BICAMS can be administered by staff members without any prior neuropsychological training in about 15 minutes.

The Symbol Digit Modalities Test (SDMT) (Smith, 1968) is thought to measure information processing speed (IPS) and one of the first cognitive functions to become impaired in MS (Van Schependom et al., 2014). The SDMT has been included in multiple batteries for cognitive impairment in MS (Benedict et al., 2002; Rao et al., 1991). The ease and short duration of the SDMT administration as well as the possibility to perform the test orally make it an ideal test to assess IPS in MS, considering effects of fatigue and reduced fine motor skills. Memory function is also frequently impaired in MS (Thornton and Raz, 1997). Although studies disagreed whether the mechanism underlying memory dysfunction was inadequate retrieval or initial learning, recent evidence supports the latter (DeLuca, Barbieri-Berger, & Johnson, 1994; John DeLuca, Leavitt, Chiaravalloti, & Wylie, 2013).

The California Verbal Learning Test-II (CVLT-II) is a measure of verbal learning and memory, and has repeatedly shown high sensitivity and specificity for memory deficits in MS (Strober et al., 2009), even when using only the first two of the five learning trials (Gromisch et al., 2013).

Finally, visuospatial memory has been frequently found to be impaired in MS (Benedict et al., 2006; Rao et al., 1991). The Brief Visuospatial Memory Test Revisited (BVMT-R)

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(Benedict, 1997) displayed high sensitivity and specificity for visual learning and memory deficits in MS (Benedict et al., 2006) and was also included in the BICAMS.

The BICAMS has already been translated and validated in Argentina (Vanotti et al., 2016), Brazil (Spedo et al., 2015), Canada (Walker et al., 2016), Czech Republic (Dusankova et al., 2012), Greece (Polychroniadou et al., 2016), Hungary (Sandi et al., 2015), Iran (Eshaghi et al., 2012), Ireland (O'Connell et al., 2015), Italy (Goretti et al., 2014) and Lithuania (Giedraitiene et al., 2015). The goal of this study was to translate and validate the BICAMS in a Dutch-speaking Belgian population, according to the international standards for validation defined by Benedict and colleagues (2012). In addition, we will provide normative data corrected for age, gender and education level for a Dutch-speaking Belgian population.

2. Material and methods

2.1 Study population

In total, 97 MS patients and 97 healthy controls were included in the study. MS patients were recruited from the National MS Center Melsbroek and the Revalidation and MS Center Overpelt in Belgium. Healthy controls were recruited from friends or relatives of MS participants and from the personnel at the MS Center Melsbroek. Healthy controls did not have experience with the tests included in the BICAMS. Criteria for inclusion were: (1) fluent in Dutch; (2) aged between 18 and 65; (3) able to provide written informed consent. Exclusion criteria were: (1) relapse in the last month before assessment; (2) neuropsychological screening in the last three months before the assessment; (3) neurological disorders other than MS that influence cognitive functioning (e.g. dementia or brain injury); (4) psychiatric disorders that could influence cognitive performance; (5) sensory or motor problems that could influence cognitive test performance. Participants did not receive any form of compensation.

2.2 Ethics

The study was approved by the ethics committee of the MS Center Melsbroek, Revalidation and MS Center Overpelt and University Hospital Brussels.

2.3 NP assessment

One examiner at each site was trained in order to ensure uniform administration, data recording and scoring. An MS-specialized nurse at the National MS Center Melsbroek, a PhD student at the Revalidation and MS Center Overpelt and a neuropsychologist at the University Hospital Brussels administered the neuropsychological tests. In order to be able to assess the added psychometric value of the full tests over the short versions included in the BICAMS, a full or extended version of the CVLT-II and BVMT-R was performed.

2.4 Neuropsychological tests

The SDMT is a measure of information processing speed, visual scanning and to a lesser extent working memory. Subjects are presented with nine symbols that are paired with the numbers one to nine. Subjects are asked to verbally respond with the paired digits as quickly

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as possible when presented with a pseudo-random sequence of symbols. The outcome measure of the SDMT is the amount of correct responses in 90 seconds.

In the CVLT-II, subjects have to recall word lists, which allows evaluation of verbal learning and memory. The examiner reads a list (list A) of 16 words, which subjects have to recall. This is repeated five times, each time with a repetition of list A. The measured outcome is the total number of words recalled over the five trials. The full version of the CVLT includes the recall of a second list (list B) after the first five trials, after which recall of list A is reassessed (short recall). Additionally, delayed recall (free recall and cued recall) and recognition (yes/no, forced choice) is assessed after 25 minutes. A Dutch translation of the CVLT-II was used.

The BVMT-R is a test of visuospatial learning and memory in which subjects have to reproduce six abstract figures in a 2 x 3 grid. Subjects are given 10 seconds to memorize the figures and their location in the grid, after which they are asked to reproduce the figures with pencil and paper, without a time limit. This is repeated for three trials. Each drawing is assigned a score of 0, 1 or 2 based on criteria of accuracy and positioning of the six figures. In the full version of the BVMT-R, delayed recall and recognition of the figures is assessed after 25 minutes.

In addition, depression and fatigue were assessed using Beck's depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Benedict, Fishman, McClellan, Bakshi, & Weinstock-Guttman, 2003) and Fatigue Scale for Motor and Cognitive Functions (FSMC) (Penner et al., 2009), both validated for Multiple Sclerosis. All tests were administered in a standardized order: (1) trial 1-3 of the BVMT-R; (2) trial 1-5, list B and short recall trials of the CVLT-II; (3) delayed recall and recognition trials of the BVMT-R; (4) SDMT; (5) BDI; (6) recall and recognition trials of the CVLT-II.

Delays between the first and short recall trials and the delayed recall and recognition trials of the CVLT-II and BVMT-R were approximately 25 minutes. These delays were, however, prone to individual differences, which could possibly have an influence on the sensitivity of the full versions of the CVLT-II and BVMT-R.

2.5 Statistical analysis

All statistical analyses were performed using R (R Core Team, 2016). Wilcoxon-Mann-Whitney, Chi-squared and t-tests were used for group comparisons. Regression-based norms were calculated in accordance with previously described procedures for MACFIMS (Parmenter et al., 2010). A statistical significance level of .05 was used and p-values were adjusted using Benjamini–Hochberg's procedure in order to correct for multiple comparisons. Inter-quartile ranges (*IQR*) were calculated using linear interpolation of modes. Cohen's *d* was calculated as effect size for parametric tests, while effect size *r* was calculated for non-parametric tests (Field, 2005).

3. Results

3.1 Study participants

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Demographic characteristics of the MS and HC group are presented in Table 1. Healthy controls were matched to PwMS on age, education level and gender. A comparison with populations from other BICAMS validation studies can be found in Additional Table 1.

Table 1. Demographic data of study sample

		MS (*n* = 97)	HC (*n* = 97)	*p*
Age (*M* ± *SD*)		45.42 ± 9.24	43.52 ± 12.69	.41
Gender (men/women)		29/68	22/75	.33
Schooling level (*M* ± *SD*)		14.28 ± 1.86	14.69 ± 1.61	.33
BDI (*M* ± *SD*)		10.26 ± 7.47	4.67 ± 4.06	<.001
EDSS (*M* ± *SD*)		3.50 ± 2.50		
Disease duration (*M* ± *SD*)		12.97 ± 7.16		
Disease type	RRMS	84%		
	PPMS	4%		
	SPMS	12%		

M = mean; *SD* = standard deviation; BDI = Beck's Depression Inventory; EDSS = Expanded Disability Status Scale; RRMS = relapsing-remitting MS; PPMS = primary progressive MS; SPMS = secondary progressive MS.

3.2 BICAMS validity

The raw scores of the HC and MS group were compared in order to validate the three BICAMS tests. Table 2 presents the mean raw scores for each test. The MS group performed significantly worse than the HC group on the SDMT and BVMT-R, corresponding to a, respectively, moderate to large and small effect size. No significant difference was found between the MS group and the HC group on the five recall trials of the CVLT-II. When inspecting the distributions of test scores using the Beanplots (Kampstra, 2008) in Figure 1, we observe a general shift downwards in the scores of the MS group compared to the HC group. For the CVLT-II, a minimal downwards shift in the 75th and 100th percentile is noticeable for the MS group. The BVMT-R scores, finally, show a minimal downwards shift (of 1 point) in the 25th and 50th (median) percentile and a large shift (of >3 points) of the 75th and 100th percentile in the MS group.

When comparing the extended BVMT-R, or the sum of the first three and the delayed recall trials, a significant difference between the MS group and the HC group with a medium to large effect size was observed. For the extended CVLT-II, the total of all recall trials was calculated as well as the recall discriminability index *d'*. This index was proposed in a study by Donders & Nienhuis (2007) and takes the amount of intrusions into account. Using both the total of all recall trials and the discriminability index *d'*, no significant difference between the MS and HC group was observed in CVLT-II performance.

Table 2. Group performances on BICAMS and alternative measures

	HC (*n* = 97)	MS (*n* = 97)	*p*	*effect size*
SDMT (*M* ± *SD*)	60.95 ± 10.21	52.11 ± 13.11	< .001	*d* = .752
CVLT-II (*Md*, *IQR*)	63, [56 – 68]	64, [54 – 70]	.573	r_{ES} = .013

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BVMT-R (*Md*, *IQR*)	29, [25 – 32]	28, [21 – 31]	.007	r_{ES} = .188
CVLT-II Full (*Md*, *IQR*)	123, [108 - 131]	122, [104 - 132]	.442	r_{ES} = .010
CVLT-II *d'* (*Md*, *IQR*)	.62, [-.27 – 1.21]	.23, [-.98 – 1.16]	.124	r_{ES} = .092
BVMT-R Full (*Md*, *IQR*)	38, [33 – 43]	31, [26 – 41]	< .001	r_{ES} = .307

Mean (*M*) or median (*Md*) raw scores and standard deviations (*SD*) or inter-quartile ranges (*IQR*) per group for each BICAMS measure and the alternative measures. Effect sizes calculated are Cohen's *d* (small: .200, medium: .500, large: .800) or effect size r_{ES} (small: .100, medium: .300, large: .500). SDMT = Symbol Digit Modalities Task; CVLT-II = California Verbal Learning Task II; BVMT-R = Brief Visuospatial Memory Test Revisited; *d'* = recall discriminability.

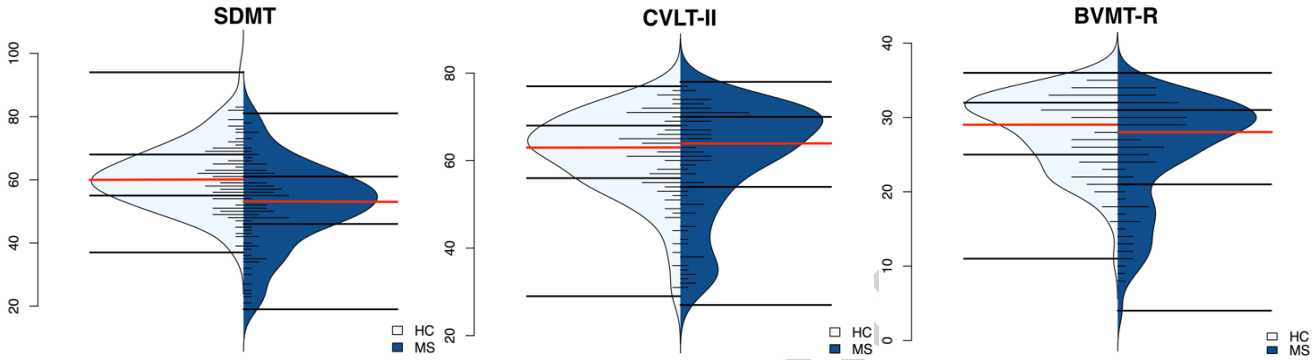

Figure 1. Beanplots illustrating the distributions of raw scores in the two groups for the three BICAMS measures. Bold horizontal lines reflect the 0, 25th, 75th and 100th percentile of the raw score distributions. For the SDMT, the bold red line represents the mean raw score for each group. For the CVLT-II, and BVMT-R, the bold red line represents the median raw score for each group. Density shapes are based on the normal density trace. Plots were made using the 'beanplot' package in R (Kampstra, 2008). SDMT = Symbol Digit Modalities Task; CVLT-II = California Verbal Learning Task II; BVMT-R = Brief Visuospatial Memory Test Revisited.

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3.3 Regression-based norms

Based on Parmenter et al. (2010), we provide regression based norms using (1) a conversion table (Table 3) from raw scores to scaled scores (*M* = 10, *SD* = 3) based on the cumulative frequency distributions from the HC group and (2) regression models for each BICAMS test (Table 4) based on data from our HC group. These regression models allow the calculation of a predicted (scaled) score based on the demographic data of each subject using the following formula (example for SDMT):

$$\widehat{score}_{SDMT} = intercept_{SDMT} + \boldsymbol{age} * \beta_{age,SDMT} + \boldsymbol{age^2} * \beta_{age^2,SDMT} + \boldsymbol{gender} * \beta_{gender,SDMT} + \boldsymbol{education} * \beta_{education,SDMT}$$

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Using this formula and the coefficients from Table 4 we can, for example, calculate the predicted SDMT score of a 42-year old female (male: gender = 1; female: gender = 2) MS patient with a bachelor's degree (15 years of education):

$$11.223 = 10.648 + \mathbf{42} * -.289 + \mathbf{422} * .002 + \mathbf{2} * -.05 + \mathbf{15} * .479$$

We can then convert the patient's actual score on the SDMT (for example 51) to a scaled score (7) using Table 3, which allows us to calculate the difference between the predicted and actual score. A z-score can be calculated by dividing the difference between the predicted scaled score and the actual scaled score by the standard error of the residual (RSE) of the regression model (Table 4). In our example, this leads to a z-score of -1.514 ((7 - 11.223) / 2.790).

$$z = \frac{(actual\ score_{SDMT} - \widehat{score}_{SDMT})}{RSE_{SDMT}}$$

Table 3. Conversion table: raw to normative scores.

Scaled score	SDMT	CVLT-II	BVMT-R
2	36-38	<39	<17
3	38-40	39-41	17-18
4	41-43	42-45	19
5	44-47	46-48	20-21
6	48-50	49-51	22-23
7	51-54	52-54	24
8	55-57	55-58	25-26
9	58-60	59-61	27-28
10	61-64	62-64	29
11	65-67	65-67	30-31
12	68-71	68-70	32-33
13	72-74	71-74	34-35
14	75-77	75-77	36
15	78-81	>78	
16	82-84		
17	85-88		
18	>88		

Conversion of raw scores of the three BICAMS measures to normative scores (M = 10, SD = 3), based on the cumulative distribution of 97 healthy controls. SDMT = Symbol Digit Modalities Task; CVLT-II = California Verbal Learning Task II; BVMT-R = Brief Visuospatial Memory Test Revisited.

Table 4. Regression models of the three BICAMS measures.

	Predictor	Coefficient *β*	Standard error *β*	*T*	*p*	Adjusted R^2	*RSE*
SDMT	Intercept	10.648	3.869	2.753	.007	.135	2.790
	Age	-.289	.190	-1.519	.132		
	Age^2	.002	.002	1.064	.290		
	Gender	-.050	.694	-.073	.942		

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	Education	.479	.190	2.524	.013		
CVLT-II	Intercept	9.052	3.894	2.324	.022	.124	2.801
	Age	-.230	.191	-1.199	.234		
	Age^2	.002	.002	.966	.337		
	Gender	2.182	.699	3.124	.003		
	Education	.323	.191	1.692	.094		
BVMT-R	Intercept	16.902	3.873	4.364	<.001	.133	2.793
	Age	-.473	.190	-2.484	.015		
	Age^2	.005	.002	2.107	.038		
	Gender	-1.427	.695	-2.054	.043		
	Education	.341	.190	1.789	.076		

SDMT = Symbol Digit Modalities Task; CVLT-II = California Verbal Learning Task II; BVMT-R = Brief Visuospatial Memory Test Revisited. RSE = Residual Standard Error

3.4 Relationships with other variables

Figure 2 displays the relationships of PwMS' performance on the three BICAMS subtests with age, EDSS, BDI and FSMC scores. The most remarkable findings are that the CVLT-II does not correlate significantly with age, and depression (assessed with BDI) and cognitive and motor fatigue (assessed with FSMC) only correlate significantly with SDMT scores.

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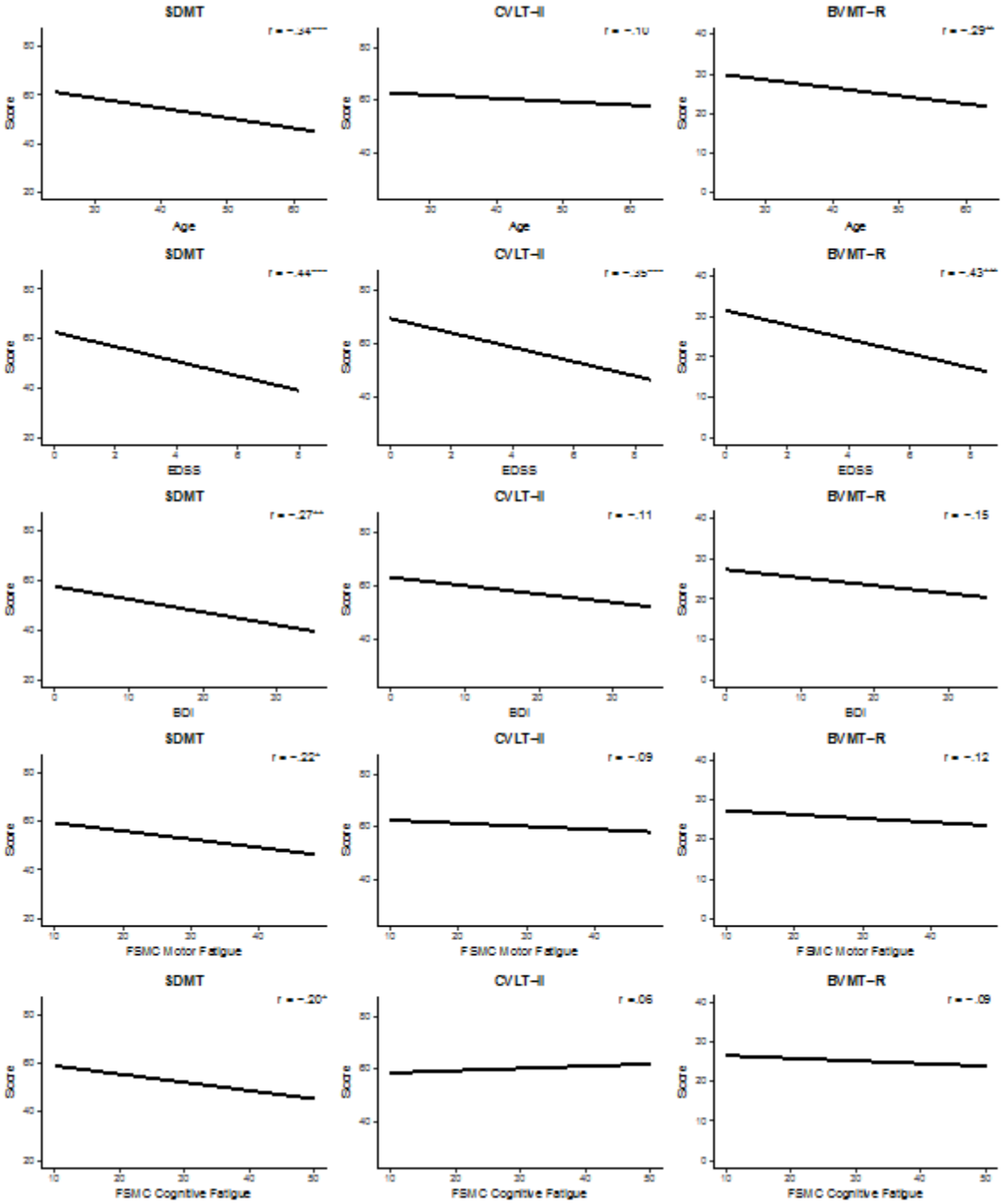

Figure 2. Correlations of the three BICAMS subtests with age, physical disability, depression and fatigue. Correlation coefficients (r) are presented in the upper right corner, with significance marks: * p < .05, ** p < .01, *** p < .001. Darker dots mark overlapping data points. Grey area illustrates the 95% confidence interval using a linear model. SDMT = Symbol Digit Modalities Task; CVLT-II = California Verbal Learning Task II; BVMT-R = Brief Visuospatial Memory Test Revisited; BDI = Beck's Depression Inventory; EDSS = Expanded Disability Status Scale; FSMC = Fatigue Scale for Motor and Cognitive Functions.

4. Discussion

The BICAMS is a reliable, neuropsychological screening battery for cognition in MS which has been validated in several languages and countries. It has major advantages over other

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neuropsychological batteries by being very fast and easy to administer, making it less tiring for patients who very often have complaints of fatigue, and easier for small MS centres without a large neuropsychological staff to assess the cognitive status of their patients.

Our validation study provides evidence for the psychometric characteristics of two of the three BICAMS measures, the SDMT and BVMT-R, and a possible explanation and solution for the lack thereof in the CVLT-II in a Belgian Dutch-speaking population. In addition, using the extended versions of the CVLT-II and BVMT-R, as used in the MACFIMS battery (Benedict et al., 2002) does not improve the psychometric properties of the BICAMS test to a large extent. Normative data for use of the BICAMS in a Belgian Dutch-speaking population is also provided.

When comparing our study sample of patients and controls with regard to age, gender balance, education level and EDSS scores to that of other validation studies, the average age appears to be higher than what is found in the majority of studies (Additional Table 1). Similar to the findings in the Czech BICAMS validation study (Dusankova et al., 2012), the SDMT and BVMT-R scores showed the largest differences between the MS and HC group.

Interestingly, the SDMT scores in the MS group show a general downward shift (see Fig. 1) while the BVMT-R scores display an asymmetric downward shift with the 75th and 100th percentile of the MS group scores showing larger differences than the 25th and 50th or median percentile. This phenomenon could be explained by recent findings by Van Schependom and colleagues (2014) who showed that visuospatial memory and learning gets impaired in later stages of the disease compared to IPS, which is thought to be the first and also most widely affected cognitive domain in MS. Taking this into account, the asymmetric downward shift in BVMT-R scores of the MS group compared to the HC group could be interpreted as a subpopulation that has started to show problems in visuo-spatial memory while the a larger subpopulation does not yet show these problems. The more general shift in SDMT scores of the MS group suggests that the largest part of them is already displaying problems with information processing speed.

Remarkably, our two groups did not show any significant difference in CVLT-II scores. Figure 1 illustrates that besides a reasonable number of MS patients that score very low (i.e. impaired), most MS patients seem to score better on the CVLT-II than the HC group. This is confirmed by a slightly higher 50th, 75th and 100th percentile score for the MS group compared to the HC group. This was surprising and in contrast with every BICAMS validation study until present (Dusankova et al., 2012; Eshaghi et al., 2012; Giedraitiene et al., 2015; Goretti et al., 2014; O'Connell et al., 2015; Polychroniadou et al., 2016; Sandi et al., 2015; Spedo et al., 2015; Vanotti et al., 2016; Walker et al., 2016). We would like to argue that this might be a consequence of learning effects, as there is a large potential for learning in the CVLT-II. First, the 16 words are repeated a large number of times (especially in the full version of the CVLT-II) so it is not impossible that subjects remember the words long after the test was acquired. Second, there is an optimal strategy that subjects can discover: semantic clustering. The 16 words can be organised in four semantic categories. It has been well known for a long time in cognitive psychology that organisation improves short-term information storage (for review see Mandler, 1967). Important for this is that in the (short and long delay) cued trials of the full CVLT-II, subjects are explicitly instructed to recall the words per category. Therefore, subjects who have performed the full version of the

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CVLT-II only once might already benefit by knowing that there are four categories and that semantic clustering might help them. A possible explanation to why other studies do not find these learning effects might be that the full version of the CVLT-II is a very frequently administered test in the recruiting centres, known as centres for multidisciplinary treatment and rehabilitation for people with MS in Belgium, that participated in this study. This might not have been the case for the other validation studies. This explanation is supported by the fact that the CVLT-II scores of our MS group are remarkably high compared to other validation studies (Additional Table 1). Unfortunately, no data is available on how many times participants were administered the BICAMS subtests. In light of these findings, we would like to stress the need for alternative word lists for the CVLT-II, similar to the different SDMT forms that are available, or the construction of an adapted version which is fitted for repeated administration.

Using the full version of the CVLT-II (r_{ES} = .092), as used in the MACFIMS, only marginally increased the difference in scores between the two groups compared to the short version (r_{ES} = .013). The full version of the BVMT-R (r_{ES} = .307) did yield better effects than the shorter BICAMS-version (r_{ES} = .188), which leads to a cost-benefit discussion. While the full BVMT-R would be able to assess cognition more completely, this test would take significantly longer (25 min. waiting time and about 5 min. of delayed recall trials) than the short version. Hence, including the full BVMT-R would abolish one of the main advantages of the BICAMS; that it can be administered in only 15 minutes. Therefore, we advise to keep the current composition of the BICAMS as a screening tool and to utilize more extensive batteries such as the MACFIMS (Benedict et al., 2002) or NSBMS (Rao et al., 1991) when more detailed cognitive assessments are required.

Finally, performance of the MS group on the SDMT and BVMT-R correlated significantly with age, as did all three subtests with physical disability (EDSS). Age, considering the difficulty of determining disease onset in MS, and physical disability can both be interpreted as a reflection of disease severity. In addition, the SDMT was the only test that correlated with depression (BDI) and cognitive and motor fatigue (FSMC). The former could be related to effects of treatment with antidepressants and is consistent with some previous findings (Arnett, 2005; Landrø et al., 2004; Vanotti et al., 2016) although some studies did not find this relationship (O'Connell et al., 2015). The latter makes sense as the SDMT is a test with a time limit and fatigue is well known to influence processing speed (Diamond et al., 2008).

Although the delays between the first and short recall trials and the delayed recall and recognition trials of the CVLT-II and BVMT-R were approximately 25 minutes (as recommended by Langdon et al., 2012), a possible limitation could be the inter-subject differences in delays, due to some subjects needing more or less time to complete the intermediate tests. It is possible that subjects who are cognitively impaired need more time for those tests and – therefore – experience a longer delay (and thus a disadvantage) in the administration of delayed recall and recognition trials. A final limitation could be the sample size. Although we included significantly more subjects (97) than recommended by Benedict et al. (2012) to validate the BICAMS and the effect size favourably compares to similar validation studies (see Additional Table 1), a larger control sample could strengthen the presented results.

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5. Conclusion

In this study, we aimed to validate the BICAMS, a screening battery for cognition in MS that is fast, easy-to-use and already widely-validated, in a Belgian Dutch-speaking population. We provide evidence for the psychometric qualities of two of the three BICAMS tests: the SDMT and BVMT-R. The CVLT-II failed to dissociate between MS patients and healthy controls, in contrast to previous BICAMS validation studies. We argue that this is a consequence of learning effects, illustrated by the score distributions in both groups. Therefore, the construction of alternate CVLT-II forms or test procedures is strongly advocated.

In addition, we showed that using the extended versions of the CVLT-II and BVMT-R tests does not notably improve the psychometric qualities of these tests as neuropsychological screening tools in MS.

Finally, we provide normative data for the use of the BICAMS in a Belgian Dutch-speaking population.

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Conflict of interest
None declared

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Additional Table 1. Population characteristics and scores of main BICAMS validation studies.

		Population size	Age (*M* ± *SD*)	Gender (% female)	Education Level (*M* ± *SD*)	Disease Duration (*M* ± *SD*)	EDSS (*M* ± *SD*)	Type MS (%RR/SP/PP/PR)	SDMT (*M* ± *SD*)	CVLT-II (*M* ± *SD*)	BVMT-R (*M* ± *SD*)
Current Study	HC	97	43.5 ± 12.7	77%	14.7 ± 1.6				61 ± 10.2	61.3 ± 9.7	28.2 ± 5.1
	MS	97	45.4 ± 9.2	70%	14.3 ± 1.9	13 ± 7.2	3.5 ± 2.5	84/12/4/0	52.1 ± 13.1	60.1 ± 12.9	25.4 ± 7.3
Dusankova et al. (2012)	HC	134	34 ± 9	71%	14 ± 2.5				65 ± 9	60 ± 8	29 ± 4
	MS	367	34 ± 10	68%	14 ± 3	8 ± 7	3 ± 1.5	68/26/3/4	50 ± 13	52 ± 11	23 ± 7
Giedraitiene et al. (2015)	HC	20	36.7 ± 16.4	33%	17.5 ± 3.5				57 ± 11.5	65.7 ± 5.9	29.6 ± 4.1
	MS	50	38.8 ± 10.2	47%	15.9 ± 2.8	11.7 ± 9.2	3.3 ± 1.3	88/6/2/4	42.7 ± 13.9	55.9 ± 10	23.1 ± 7
Goretti et al. (2014)	HC	273	38.9 ± 13	52%	14.9 ± 3.1				56.3 ± 11.3	56.3 ± 9	27.9 ± 6.1
O'Connell et al. (2015)	HC	66	43.9 ± 12.1	73%	13.6 ± 2.7				56.1 ± 10.6	53.6 ± 9.1	20.9 ± 6.5
	MS	67	42.7 ± 12.8	68%	14.1 ± 3.1	N.A.	1.8 ± 0.9	70/28/2/0	46.0 ± 12.9	45.3 ± 10.2	17.9 ± 7.1
Polychronia dou et al. (2016)	HC	79	36.2 ± 10.6	60%	15.6 ± 5.5				61.4 ± 13.1	60.5 ± 10.7	22.1 ± 6.5
	MS	44	40.2 ± 9.9	61%	13.9 ± 4.2	N.A.	3.5 + N.A.	83/10/8/0	45.0 ± 17.2	55.5 ± 12.3	18.5 ± 8.3
Sandi et al. (2015)	HC	65	40.9 ± 11.8	75%	N.A.				66.2 ± 12.4	59.0 ± 8.3	26.7 ± 5.6
	M	65	41.	75%	N.A.	11.1 ±	2.5	100/0/0/0	55.6	55.4	22.5

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	S		9 ± 8.9			7.6	± 1.8		± 15.5	± 10.7	± 8.5
Spedo et al. (2015)	HC	58	40.3 ± 11.9	55%	12.5 ± 3.6				47.5 ± 13	53.4 ± 10.8	23.8 ± 7.7
	MS	58	41.2 ± 12.2	69%	12.7 ± 5.2	8.3 ± 6.6	4.2 ± 2	100/0/0/0	35.9 ± 16.1	42.1 ± 12.4	19.9 ± 8.6
Vanotti et al. (2016)	HC	100	42.4 ± 10.1	75%	14.9 ± 2.5				56.7 ± 10.9	60.9 ± 10.5	23.4 ± 5.8
	MS	50	43.4 ± 10.2	74%	14.9 ± 2.8	13.1 ± 9.1	3.3 ± 2.6	78/9/4/0	45.1 ± 16.1	50.9 ± 12.4	20.7 ± 7.74
Walker et al. (2016)	HC	51	41.9 ± 10.8	86%	16.31 ± 2.1				59.1 ± 8.5	57.7 ± 7.9	29.8 ± 3.6
	MS	51	45.4 ± 9.9	80%	15.44 ± 2.7	10.11 ± 7.7	2.7 ± 1.9	77/16/7/0	49.7 ± 10.8	51.6 ± 10.1	24.6 ± 6.5

M = Mean; *SD* = Standard Deviation; N.A. = data not available; RR = Relapsing-Remitting; SP = Secondary Progressive; PP = Primary Progressive; PR = Progressive-Relapsing; SDMT = Symbol Digit Modalities Task; CVLT-II = California Verbal Learning Task II; BVMT-R = Brief Visuospatial Memory Test Revisited.

Highlights

- This study validates the BICAMS in a Belgian Dutch-speaking population
- Including full versions of the CVLT-II and BVMT-R does not increase performance
- MS patients and HCs show differences on the SDMT and BVMT-R but not on the CVLT-II
- CVLT-II scores of MS patients suggest strong learning effects

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