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## 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

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### Abstract

**Background:** Multiple Sclerosis (MS) causes not only somatic, but also cognitive impairment regardless of the patients' age or the course of the disease. The Brief International Cognitive Assessment for MS (BICAMS) test, published in 2011, is a short cognitive questionnaire: a fast, reliable, sensitive and specific tool for the evaluation of the patients' cognitive state.

**Objectives:** Our primary objective was to assess the validity of the Hungarian version of the BICAMS test. Our secondary objective was to evaluate the impact of the cognitive impairment on the patient's quality of life and fatigue's impact on the patients' cognitive state.

**Methods:** 65 RR-MS patients and 65 age, sex and education matched healthy control (HC) subjects completed the test and were retested after 3 weeks. The patients also completed the MS Quality of Life 54 (MSQoL54) and the Fatigue Impact Scale (FIS) assessments. Group differences were calculated by paired sample T-tests. The test-retest reliability was measured by intraclass correlation coefficients. To analyze the difference between the test-retest performances of the two groups we used two-way repeated measures ANOVA where the BICAMS battery was the single composite outcome and one-way repeated measures ANOVA. To assess the impact of the cognitive decline on the patients' quality of life and fatigue's impact on the cognitive state, we examined the correlations between results in the BICAMS and the MSQoL54 and FIS.

**Results:** We found significant difference ( $p \leq 0.001$ ,  $p = 0.017$  in the first CVLT-II assessment) between MS patients and members of the HC group in all four evaluated parameters of BICAMS test in both sessions. The correlation coefficients were very strong between the tests and retests ( $r > 0.8$ ;  $p < 0.001$ ;  $r = 0.678$ ,  $p < 0.001$  between the CVLT-II assessments). We found that the HC group performed significantly ( $p = 0.020$ ) better in the retest sessions as compared to their original performance than the patients did and this difference is solely due to the difference between the CVLT-II performances. We have found significant negative correlation between the patients' cognitive function and the fatigue score ( $r < -0.3$ ,  $p < 0.05$ ). Seven of the MSQoL-54 subscales correlated with the BICAMS performance ( $r > 0.3$ ;  $p < 0.05$ ).

**Conclusions:** The Hungarian version of the BICAMS test is a valid and reliable method for the evaluation of MS patients' cognitive function. It seems that because of the short retest period, the members of the HC group remembered the CVLT-II words thus performed better than the patients did. Also apparently fatigue can have a negative impact on the patients' cognitive state, and cognitive impairment could worsen the patients' quality of life.

**Keywords:** Multiple Sclerosis, Cognition, Validation, BICAMS, Fatigue, Health-related quality of life

## ***Introduction***

Multiple Sclerosis (MS) is a chronic, autoimmune and neurodegenerative disease of the central nervous system (CNS) which can cause a wide range of symptoms, including decline in the cognitive functions. The prevalence of cognitive impairment is found to be high in MS patients, ranging from 43-70 % . It can occur at all stages of the disease, even in clinically and radiologically isolated syndromes (CIS and RIS) and can affect any patient regardless of age and sex .

Cognitive impairment is not global in MS; it most commonly affects three aspects: information processing speed being the most vulnerable aspect followed by episodic memory and executive function . The degree of the impairment can be mild and patients may not be fully aware of it . Also patients often report the cognitive decline unreliably as depression can cause over-reporting, while metamemory-impairment can lead to underestimation .

There is significant correlation between the progression of cognitive impairment and the rate of brain atrophy according to studies involving magnetic resonance imaging (MRI) in the evaluation . Also the presence of cortical lesions is associated with the decline in cognition .

Fatigue is a very common symptom of MS; studies indicate its prevalence to be 76-92% . Many patients report it to be the worst or one of the worst symptoms of the disease . Studies show significant correlations between the Expanded Disability Status Scale (EDSS) score and fatigue's presence and severity . Hypothetically fatigue can have a negative impact on the patients' cognitive abilities, though recent studies did not find significant correlation between cognitive status and subjective fatigue .

Health-related quality of life (HRQoL) by definition represents "the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient" . In the different clinical courses of MS differences were found between the subgroups: quality of life was lower of the patients with longer disease duration and with a more severe and progressive clinical course . Cognitive impairment is an extremely important aspect of HRQoL as it is an important determinant of employment status and social costs . Also cognitive deficit impairs the patients' activities in everyday life by reducing physical independence, driving ability, coping, symptom management and rehabilitation potential . It was found that MS patients are more concerned about their mental health than physical disability .

The importance of assessing the cognitive status of patients with MS cannot be overstated. There are several psychometric assessment batteries available, the most frequently utilized are the Brief Repeatable Battery of Neuropsychological tests (BRB-N) and the Minimal Assessment of Cognitive Function in MS (MACFIMS) . The problem with these batteries are that they are time-consuming (BRB-N requires 45 minutes, MACFIMS approximately 90

minutes to perform) and they require special expertise which is not routinely available in many places . For this reason a specialized battery has been recommended by the BICAMS committee, which is short, simple to administer and to score, and does not require any special equipment or training but is also highly sensitive .

## ***Objectives***

The objectives of our study were:

1. The cross-cultural validation of the BICAMS battery to Hungarian language.
2. Measuring the impact of cognitive impairment on the patients' quality of life and fatigue's effect on the patients' cognitive state by assessing the correlations between BICAMS performance with the Hungarian versions of both the FIS and MSQoL-54 batteries.

## ***Patients and methods***

### **Methods**

The BICAMS battery comprises of 3 individual tests: the Symbol Digit Modalities Test (SDMT), the first five recall trials of the California Verbal Learning Test II. (CVLT-II) and the first three recall trials of the Brief Visuospatial Memory Test Revised (BVRT-R) .

The SDMT measures the information processing speed of the participant. It is a sheet of nine symbols in pseudo-randomized lines, each paired with a digit in a key at the top of the sheet. After a short practice, the patients have to pair as many of the symbols with the digits as they can in 90 seconds. There is both a written and an oral version of the test. During the written version the patients are given the sheet and they have to write the correct digits on the paper, whereas in the oral version both the administrator and the patient are given one sheet each and the patient is required to say the correct number out loudly while the administrator writes it down. Both versions of SDMT were administered for the capability to assess patients with impaired motor functions. The dependent variable is the total number of correct responses .

The CVLT-II is a tool for measuring verbal learning. The first five recall trials of CVLT-II are comprised of a list of 16 words clustered into 4 semantic groups. During administration the administrator reads the list aloud at the approximate speed of 1 word/second. The patients have to recall as many of the words as they can and repeat them back to the administrator in arbitrary order, who writes them down. There is no time limit for this test. The dependent variable is the total number of correct words recalled during the five trials .

The BVRT-R is the measure of visual memory. It is administered by giving the patients a blank sheet of paper divided into six equal parts and a pencil. Then the administrator shows them a matrix of 6 abstract designs for 10 seconds which the patients are required to reproduce on the blank sheet of paper as accurately as they can. Each design receives a score of 0, 1, or 2 based on accuracy and location criteria. There is no time limit for this test. The dependent variable was the total points received for the reproduced designs during the three trials .

The validation was conducted per the international standards given by Benedict et al. in 2012 . As the first step, the CVLT-II list of words were translated and retranslated from English to Hungarian and vice versa respectively (the other two tests did not require translation due to their nature). In the second step, the relevant parts of the tests manuals were translated into

Hungarian. The third step was the testing, and after 3 weeks, the retesting of the patients and members of the HC group matched in age, sex and years of education between December 2013 and March 2014.

Also for the assessment of the correlations between the cognitive status and fatigue and the cognitive status and quality of life, all 65 patients had completed the Hungarian versions of the Fatigue Impact Scale (FIS) and the Multiple Sclerosis Quality of Life-54 (MSQoL54) batteries during that period.

The FIS battery is comprised of 40 questions, divided into 3 subscales: 20 questions related to social functions, 10 questions to physical functions and 10 questions to cognitive functions. Each question is marked from 0 (minimal degree) to 4 (severe degree) points .

MSQoL-54 is a battery of 54 questions which can be divided into numerous subscales representing many aspects of life: physical health, emotional well-being, role limitations due to physical problems, role limitations due to emotional problems, pain, energy, health perceptions, social function, cognitive function, health distress, sexual function, satisfaction with sexual function, change in health and overall quality of life. From these subscales, two composite scores can be derived: the physical health composite score and the mental health composite score

We used the first BICAMS tests of the patients for comparison with FIS and MSQoL-54.

### **Patients and the HC group**

We recruited 65 patients treated at the Multiple Sclerosis Outpatient's Unit of the Department of Neurology of the University of Szeged and 65 healthy controls matched in age, sex and years of education for the validation process. The patients were recruited cross-sectionally, there was no pre-selection applied for cognitive impairment. Of the patients 16 were men, 49 women; 31 of the patients studied  $\leq 12$  years, and 34 of them studied for at least 13 years. Their average age was 41.9 ( $\pm 8.9$ ) years, the average age for disease onset was 29.8 ( $\pm 9.9$ ) years and the average time from MS onset was 11.1 ( $\pm 7.6$ ) years. Their average EDSS score was 2.5 ( $\pm 1.8$ ). Of the 65 members of the HC group, 16 were men and 49 women; 31 of them studied  $\leq 12$  years, and 34 of them studied for at least 13 years. Their average age was 40.9 ( $\pm 11.8$ ) years.

We have included patients and healthy control individuals aged between 18-65 years. Their first language is Hungarian, and all the patients were diagnosed with the relapsing-remitting (R-R) course of the disease by McDonald's criteria. All patients were in remission during the evaluation and their EDSS score ranged from 0-6.5.

We have excluded patients suffering from CIS, secondary or primary progressive course of the disease in order to work with a homogenous population for statistical reasons. As progressive MS patients only total up to 20% of the population in Hungary , their numbers would not have been representative in a patient pool of 65. We also excluded patients undergoing acute infection or an acute relapse. It was observed that psychiatric diseases, mood disorders and personality disorders have a fairly large co-incidence with MS (the leading co-morbidity being depression) . As it is also established that these disorders can cause cognitive impairment , any patient or possible member of the HC group with diagnosed psychiatric, mood or personality disorder was excluded from our study. Also it was published recently that chronic alcohol abuse has a high prevalence among MS patients (14.8%) .

Chronic alcoholism severely impairs the cognitive state , therefore any patients or possible member of the HC group, with history of chronic alcohol abuse, were excluded from participation in the validation process.

## **Statistical analysis**

To measure the differences between the patients and members of the HC group we used paired sample T-tests. Assessing the test-retest reliability and the correlation between BICAMS and FIS and BICAMS and MSQoL54 were done by calculating the Pearson correlation coefficients. To analyze the difference between the test and retest performances of the patients and the HC group we used two-way repeated measures ANOVA with the result of the BICAMS battery being a composite outcome and one-way repeated measures ANOVA to assess the differences by the battery-types that compose the BICAMS battery. Statistical analysis was done by using SPSS 21.0 software.

The assessment was authorized by the Ethics Committee of the University of Szeged (authorization number 127/2013).

## **Results**

### **BICAMS validity**

Both the patients and the HC group consisted of 16 men and 49 women, in both groups 31 individuals studied  $\leq 12$  years, and 34 of them studied for at least 13 years. There was no difference between the mean age of the two groups ( $p=0.610$ ).

Table 1 shows the group data and the differences between the patients' and HC groups' raw scores in all 4 trials and during the retests as well. It is apparent that the MS patients performed significantly worse in all trials than the members of the HC group ( $p \leq 0.001$  in all tests other than the first CVLT-II;  $p=0.017$  in the first CVLT-II).

We identified 34 of the 65 (52.3%) patients with cognitive impairment, by the proposed criterion of "one or more abnormal tests". As no validated threshold of cognitive impairment for BICAMS was available, we used the thresholds given in the manuals of the separate tests (SDMT, BVMT-R, CVLT-II).

We have found that 26 patients (40.0%) had abnormal SDMT scores, 24 (36.9%) patients had abnormal BVMT-R tests and 9 (13.8%) patients' performance was abnormal during CVLT-II testing. Per the "one or more abnormal tests" criterion we found 15 patients (23.0%) with one abnormal test, 13 patients (20.1%) with two abnormal tests and 6 patients (9.2%) with three abnormal tests.

We identified 9 (13.8%) patients with abnormal score only in their SDMT performance, 6 (9.2%) only in their BVMT-R tests. We found no patient with sole CVLT-II abnormality. Ten (15.5%) patients performed impaired in both the SDMT and the BVMT-R tests, 1 (1.5%) patient in both the SDMT and CVLT-II tests, 2 (3.1%) patients in both the BVMT-R and CVLT-II tests. 6 (9.2%) patients had abnormal scores in all three tests.

**Table 1 - Group data comparing patients with multiple sclerosis and healthy controls**

|                     | Raw score ( $\pm$ SD) |                      | p      |
|---------------------|-----------------------|----------------------|--------|
|                     | Patients              | HC group             |        |
| SDMT written        | 44.31 ( $\pm$ 11.76)  | 54.88 ( $\pm$ 10.32) | <0.001 |
| SDMT written retest | 49.38 ( $\pm$ 14.91)  | 62.31 ( $\pm$ 12.78) | <0.001 |
| BVMT-R              | 22.54 ( $\pm$ 8.54)   | 26.68 ( $\pm$ 5.56)  | 0.001  |
| BVMT-R retest       | 26.89 ( $\pm$ 8.21)   | 31.81 ( $\pm$ 4.13)  | <0.001 |
| SDMT oral           | 55.62 ( $\pm$ 15.48)  | 66.82 ( $\pm$ 12.44) | <0.001 |
| SDMT oral retest    | 59.40 ( $\pm$ 18.29)  | 72.84 ( $\pm$ 13.88) | <0.001 |
| CVLT-II.            | 55.37 ( $\pm$ 10.71)  | 59.03 ( $\pm$ 8.29)  | 0.017  |
| CVLT-II. retest     | 61.77 ( $\pm$ 14.20)  | 70.58 ( $\pm$ 8.29)  | <0.001 |

SD, standard deviation; HC group, healthy control group; SDMT, Symbol Digit Modalities Test; CVLT-II., California Verbal Learning Test II.; BVMT-R, Brief Visuospatial Memory Test Revised (BVMT-R)

Table 2 shows the correlation between the tests and the retests. Overall correlations are very strong ( $r > 0.8$   $p < 0.001$ ;  $r = 0.678$ ;  $p < 0.001$  between the CVLT-II assessments). Regarding the performance of the patients and the HC group separately, the patients' performance shows slightly higher values than the HC group, the biggest difference being in the CVLT-II test ( $r = 0.743$ ;  $p < 0.001$  in case of the patients,  $r = 0.453$ ;  $p < 0.001$  in case of the HC group).

**Table 2 - Correlation coefficients between the tests and the retests**

|              | Overall |        | Patients |        | HC group |        |
|--------------|---------|--------|----------|--------|----------|--------|
|              | r       | p      | r        | p      | r        | p      |
| SDMT written | 0.874   | <0.001 | 0.883    | <0.001 | 0.796    | <0.001 |
| BVMT-R       | 0.864   | <0.001 | 0.873    | <0.001 | 0.805    | <0.001 |
| SDMT oral    | 0.830   | <0.001 | 0.884    | <0.001 | 0.664    | <0.001 |
| CVLT-II      | 0.678   | <0.001 | 0.743    | <0.001 | 0.453    | <0.001 |

HC group, healthy control group; SDMT, Symbol Digit Modalities Test; CVLT-II., California Verbal Learning Test II.; BVMT-R, the Brief Visuospatial Memory Test Revised (BVMT-R)

We evaluated the difference between the patients' and the HC group's test-retest scores. There are greater differences between the test and the retest mean scores in the HC group than between the patients' scores (Table 1) and also the correlation between the tests and the retests are weaker within the HC group as was mentioned above (Table 2).

We found significant difference between the patients' and the HC group's test-retest performances with a multivariable test where the result of the BICAMS battery was the single composite outcome ( $p = 0.020$ , Table 3). We also conducted multiple univariate tests sorting by the battery types and we found significant difference only in the CVLT-II performances ( $p = 0.003$ , Table 4). Our model satisfied the assumption of sphericity ( $p > 0.05$ ).

**Table 3 – Multivariable test of the test-retest performances of the patients and HC group**

| Within subject effect            | p      | Observed power |
|----------------------------------|--------|----------------|
| Test-Retest and Patient-HC group | 0.020* | 0.790          |

HC group, healthy control group

\*=Significant at the level of  $p < 0.05$

**Table 4 – Univariate tests of the test-retest performances of the patients and HC group by battery types**

| Within subject effect             | Measure             | p      | Observed Power |
|-----------------------------------|---------------------|--------|----------------|
| Test-Retest and Patients-HC group | <u>SDMT written</u> | 0.063  | 0.460          |
|                                   | <u>BVMT-R</u>       | 0.313  | 0.171          |
|                                   | <u>SDMT oral</u>    | 0.231  | 0.223          |
|                                   | <u>CVLT-II</u>      | 0.003* | 0.862          |

HC group, healthy control group; SDMT, Symbol Digit Modalities Test; CVLT-II., California Verbal Learning Test II.; BVMT-R, the Brief Visuospatial Memory Test Revised (BVMT-R)

\*=Significant at the level of  $p < 0.05$

### Correlations with fatigue and quality of life

We assessed the impact of subjective fatigue on the patients' cognitive status by examining the correlations between their scores during the BICAMS battery and the scores of the FIS battery.

We have found significant negative correlations ( $r < -0.3$ ;  $p < 0.05$ ) between the patients' overall subjective fatigue scores and their cognitive performance in all parts of BICAMS, shown in Table 5. Though we made the observation, that regarding the subscales, the decline in the cognitive functions measured by BICAMS correlated best with the physical dimension subscale of FIS, then with the social subscale; while considering the cognitive subscale of FIS we only found significant correlation with the oral SDMT and the CVLT-II performance.

**Table 5 - Correlations between the FIS battery and its subscales with the parts of the BICAMS battery**

|                     | Total points |        | Cognitive dimension |        | Physical dimension |         | Social dimension |        |
|---------------------|--------------|--------|---------------------|--------|--------------------|---------|------------------|--------|
|                     | r            | p      | r                   | p      | r                  | p       | r                | p      |
| <b>SDMT written</b> | -0.346       | 0.008* | -0.248              | 0.052  | -0.406             | 0,001*  | -0.293           | 0,023* |
| <b>BVMT-R</b>       | -0.322       | 0.014* | -0.247              | 0.053  | -0.351             | 0,006*  | -0.255           | 0,049* |
| <b>SDMT oral</b>    | -0.359       | 0.006* | -0.279              | 0.028* | -0.411             | <0,001* | -0.239           | 0,065  |
| <b>CVLT-II.</b>     | -0.301       | 0.022* | -0.311              | 0.014* | -0.302             | 0,018*  | -0.316           | 0,014* |

SDMT, Symbol Digit Modalities Test; CVLT-II., California Verbal Learning Test II.; BVMT-R, the Brief Visuospatial Memory Test Revised (BVMT-R)

\*=Significant at the level of  $p < 0.05$

Assessment of the impact of cognitive impairment on the patients' quality of life was done by examining the correlations between the performance in BICAMS battery and the scores in MSQoL-54.

**Table 6 - Correlations between performance in BICAMS battery and score in MSQoL-54 battery**

| MSQoL-54 scale                       | SDMT written |        | BVMT-R |       | SDMT oral |        | CVLT-II |       |
|--------------------------------------|--------------|--------|--------|-------|-----------|--------|---------|-------|
|                                      | r            | p      | r      | p     | r         | p      | r       | p     |
| Physical functioning                 | 0.440        | <0.001 | 0.279  | 0.025 | 0.427     | 0.001  | 0.252   | 0.045 |
| Cognitive functioning                | 0.300        | 0.015  | 0.298  | 0.016 | 0.302     | 0.014  | 0.325   | 0.008 |
| Social functioning                   | 0.252        | 0.043  | 0.326  | 0.008 | 0.331     | 0.007  | 0.334   | 0.005 |
| General health                       | 0.448        | <0.001 | 0.396  | 0.001 | 0.441     | <0.001 | 0.375   | 0.002 |
| Overall quality of life              | 0.251        | 0.045  | 0.273  | 0.029 | 0.280     | 0.025  | 0.239   | 0.057 |
| Sexual functioning                   | 0.445        | <0.001 | 0.332  | 0.010 | 0.461     | <0.001 | 0.402   | 0.002 |
| Satisfaction with sexual functioning | 0.391        | 0.002  | 0.337  | 0.009 | 0.402     | 0.002  | 0.376   | 0.003 |

SDMT, Symbol Digit Modalities Test; CVLT-II., California Verbal Learning Test II.; BVMT-R, the Brief Visuospatial Memory Test Revised (BVMT-R)

Table 6 shows that cognitive impairment correlates significantly with 7 subsequent subscales: physical functioning, social and cognitive functioning, general health scale, overall quality of life and sexual performance and satisfaction with sexual performance.

### ***Discussion***

Cognitive impairment is a frequent yet not routinely assessed symptom of multiple sclerosis . A special committee of neurologists and neuropsychologists has recommended the simple yet highly reliable BICAMS for assessing cognitive impairment in patients with MS . Our validation process found significant differences ( $p \leq 0.001$  in all tests other than the first CVLT-II;  $p = 0.017$  in the first CVLT-II) between the patients' scores and the scores of the members of the HC group, also it has established strong correlations ( $r > 0.67$ ,  $p < 0,001$ ) when assessing the test-retest reliability. With this method we have shown that the Hungarian version of the BICAMS battery is just as valid as the original English and recently validated Czech counterparts .

We have also evaluated the possible reason behind the slightly weaker CVLT-II correlation and the differences between the test-retest scores and the correlation coefficients of the patients and the HC group. We have found that the members of the HC group performed significantly ( $p = 0.020$ ) better at the retest period comparing to their original performance than the patients did. This difference can seemingly solely be attributed to their CVLT-II ( $p = 0.003$ ) performances, though we found a borderline significance of the within-subject effect of the written SDMT scores ( $p = 0.063$ ) with a relatively lower observed power value



( $OP=0.460$ ), which could very well mean that the lack of power is responsible for the lack of true significance. This could imply that the difference may be attributed partly to the SDMT performances as well, yet the only true significant difference was between the two groups CVLT-II scores. The reason can very well be the short interval between re-administering and the use of the same form of the CVLT-II both times, hence the examinees remembered the words from the previous examination three weeks before. Another important factor can be the lack of novelty effect during the second administration, thus the anxiety of a new situation did not interfere with the performance of the examinees. As the control group consisted of healthy individuals while more than half (52%) of the patients had cognitive impairment it is a possibility that - despite the relative better performance of the MS patients during the retest period comparing to their original scores – cognitive impairment prevented them from improving as much as the healthy individuals did, but this cannot be stated without further assessment.

Studies estimate the prevalence of cognitive impairment to be 43-70% among patients with MS. Recently, Dusankova et al. found the prevalence of cognitive impairment in the Czech MS population to be 55% while validating the Czech version of MACFIMS and BICAMS. As there was no consensus yet established, they have proposed the using of “one or more abnormal tests” for identifying cognitive deficit. By using this proposed criterion, we have found that 52% of our patients had cognitive impairment – similarly to their findings and other studies in the literature.

A relationship between fatigue and cognitive decline has been proposed, but there haven't been many studies dedicated to it. Patients often report that fatigue impairs their cognitive abilities, yet most of the studies dedicated to assess the relation between self-reported fatigue and objective cognitive performance have failed to find any significant correlation between the two. However Andreasen et al. did report that fatigued MS patients' information processing speed was slower than non-fatigued patients'. Our findings may imply similarly as Andreasen et al., that fatigue can have a negative impact on the patients' cognitive state: overall FIS points showed significant negative correlations with the patients' BICAMS performance ( $r < -0.3$ ;  $p < 0.05$ ), and the strongest correlation was shown with the SDMT performances of the patients. Yet to draw any clear conclusions, this should be investigated further on a larger population of patients by multivariable models as age, disability, disease duration and other factors could be (at least partially) responsible for the correlation. Regarding the subscales of FIS, the physical subscale showed the strongest correlation with cognitive status and the cognitive subscale only showed significant correlation with the oral version of SDMT and the CVLT-II tests. This could imply that the physical aspect of fatigue could be primarily responsible for the worsening, but as said above, clear conclusions cannot be drawn without further investigations. As was mentioned, it is important that our patient pool was comprised of only 65 patients, so evaluation on a larger population might yield different results. Also we only assessed patients of the relapsing-remitting disease course and it has been suggested that cognitive impairment might be a corresponding marker of the progressive component of MS, so future evaluations should take this into consideration.

Multiple Sclerosis affects the patients' quality of life on several levels, and the impact of cognitive impairment on the patients' HRQoL is a highly important problem. As MS patients have a high prevalence of cognitive dysfunction, and it was shown that MS patients are more concerned about their mental status than their physical disability, the correlation between their cognitive performance and their self-reported quality of life becomes a very important question. Several studies found that the decline in cognitive status worsens the patients QoL.

Benito-León et al. reported that during their evaluation, QoL significantly correlated with cognitive status, depression and anxiety - which means that the worse the cognitive performance is, the lower the patient's QoL is. Interestingly however during the COGIMUS study, they only found significant difference between cognitively impaired and cognitively healthy MS patients in two subscales of MSQoL-54 and the cognitively impaired patients reported better QoL. Also Kenealy et al. observed that MS patients with impaired autobiographical memory reported significantly better HRQoL. However it is known that high cognitive reserve (which was the case in COGIMUS as mean IQ was over 102) protects from cognitive decline and may suggest better coping mechanisms which can lead to better perception of QoL. Kenealy et al. concluded that patients with impaired autobiographical memory may not be able to validly compare their past QoL to the present which can result in these findings.

Our findings yielded similar results as the studies mentioned earlier. Seven subscales of MSQoL-54 showed significant correlation with scores on the BICAMS battery – cognitive, physical and social functioning subscales, overall quality of life and general health subscales, the sexual function and the satisfaction with sexual function subscales showed significant  $r$  levels. This means that cognitive impairment may be responsible for a serious negative impact on the patients' QoL and not just in some aspects of life, but in most. Though, as well as fatigue's impact on cognition, this should be evaluated on a larger patient pool and more variables (demographic, co-morbidity etc.) should be considered.

As a conclusion we can state that the Hungarian version of BICAMS, which is the third version to be validated in Europe, is a short, easily administered yet highly sensitive and specific tool for clinical evaluation of the cognitive impairment in MS. Also our findings suggest that fatigue can have a negative impact on the patients' cognitive state and that the decline in cognition could damage the patients' quality of life. Therefore the assessment and the follow-up of the patients' cognitive status should be as much a priority as the evaluation of somatic manifestations of the disease.

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