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Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS): Canadian contribution to the international validation project

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ABSTRACT

Background: Given the high prevalence of cognitive dysfunction in people with multiple sclerosis (PWMS) and the lack of availability of specialized neuropsychological services in most MS Clinics, there is a need for a brief cognitive monitoring tool that can be easily administered by MS clinic staff.
Objective: We aimed to establish the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) as a feasible cognitive monitoring tool and provide Canadian data toward the international validation effort. Secondary considerations were to determine if BICAMS correlates with self-reported cognition and predicted vocational status.
Methods: 57 PWMS were matched to 51 healthy controls (age, sex, education). Participants completed the BICAMS battery which includes the Symbol Digit Modalities Test, and the learning trials from the California Verbal Learning Test-II and the Brief Visuospatial Memory Test-Revised. Depression, self-reported cognition, and fatigue were assessed. Participants were re-tested 15.6 (SD 2.0) days later.
Results: With impairment defined as "one or more abnormal tests," 57.9% of MS sample was cognitively impaired. Participants were more likely to be impaired on the BVMT-R (43.9%). On the SDMT and CVLT-II, 28.1% and 26.3% of MS participants were impaired. Sensitivity and specificity were highest for the SDMT. The BICAMS was reliable over time (r value range from 0.69 for BVMT-R to 0.87 for SDMT) with the SDMT being most robust. There was no relationship between BICAMS and subjective cognition. The BVMT-R reliably predicted employment.
Conclusions: The BICAMS detected cognitive impairment to a comparable degree to more comprehensive neuropsychological batteries and is a valid measure of cognition in MS. Reliability of components varies, suggesting care be taken when interpreting serial testing results. The BICAMS is a feasible cognitive assessment tool in Canadians and yields comparable results to other cultures.

1. Introduction

Cognitive dysfunction is present in up to 70% of people with MS [1]. The strong negative impact on health-related quality of life (HRQL) that accompanies cognitive impairment in people with MS (PWMS) [2–6] makes it essential to identify the impairment early so that steps can be taken to alleviate some of the associated suffering. Given that specialized neuropsychological services to address this issue are not available in most settings due to resource issues or prohibitive cost, there is a necessity for screening tools that can be used in MS Clinics or physicians' offices to identify those with cognitive impairment. Given the subtleties of the cognitive deficits in some instances, they are not easily identified in standard clinic or physician visits [7]. Thus, the development and implementation of cognitive monitoring tools is gaining widespread interest in the literature given the clear clinical need [8–10].

In response to this need, the Brief International Cognitive Assessment for MS (BICAMS) initiative was undertaken [11]. The goal was to bring together a panel of experts in the cognitive aspects of MS to recommend a brief, cognitive assessment for MS that can be used in centers with staff members who may not have neuropsychological training. The tests that were recommended for the BICAMS battery were chosen by the panel on the basis of their psychometric qualities (reliability, validity, and sensitivity), international application, ease of administration, feasibility in the specified context, and acceptability to patients [11].

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Particular heed was given to the need for tests that addressed the areas of cognitive deficit that are typically observed in MS. The BICAMS can be administered in 15 min.

Evidence suggests that the primary cognitive deficit in MS may be an impaired ability to process information as quickly as healthy individuals [12–19]. Longitudinal studies suggest that information processing speed may be a good predictor of long-term cognitive impairment [20]. Thus, the Symbol Digit Modalities Test (SDMT) [21] was chosen for the BICAMS battery given that it has proven to be a psychometrically sound measure that is sensitive to these deficits and is both easily and rapidly administered. It is more palatable to people with MS [22] than the other commonly used measure of information processing speed in MS (Paced Auditory Serial Addition Test). The SDMT is already included in lengthier batteries designed for MS [23–25] and equivalent alternate forms are available [26]. The oral version of the task was selected to ensure that reduced fine motor skills (often associated with MS) does not confound performance.

Memory deficits are also common in MS. These difficulties are primarily during the encoding or learning phase given that retrieval typically reaches normal limits with adequate encoding [27–29]. The California Verbal Learning Test-II (CVLT-II) [30] is a standard measure of verbal learning and memory in clinical neuropsychology. Consistent with the expected encoding deficits, the CVLT-II total learning score was found to be sensitive to the memory deficits in MS and was able to discriminate MS patients from healthy controls [25]. Indeed, even when only the first two of the five learning trials were used, verbal memory problems in MS were accurately identified [10]. The third and final BICAMS measure is the Brief Visuospatial Memory Test-Revised (BVMT-R) [31]. This is again a well-established measure of visual learning and memory in MS, has been demonstrated to discriminate well between those with MS and healthy controls [32] and demonstrates good test–retest reliability when used for repeated assessments [33]. As with the CVLT-II, only the learning trials are administered given the good psychometric properties [31] and the demonstrated association with neuroimaging variables measuring lesion volume and atrophy [34–36].

International standards for validation have been established [37] and efforts are being made to validate BICAMS across a number of different countries. A Persian translation was developed and validated in Iran [38] on the entire MACFIMS (Minimal Assessment of Cognitive Function in MS) battery (of which BICAMS is a subset of tests) with 158 PWMS with either relapsing–remitting or secondary progressive course matched to 90 healthy controls. All tests were able to discriminate between groups, with ROC analyses demonstrating that the SDMT had the best sensitivity and specificity (area under the curve, AUC = 0.90). The sensitivity of the CVLT-II and the BVMT-R were essentially equivalent (AUC = 0.86 and 0.83, respectively). A similar validation study on a Czech translation [39] was completed with 369 individuals with all subtypes of MS compared to 134 healthy controls. Cognitive impairment was defined as impaired (greater than 1.5 SD from the mean) performance on "one or more of the three BICAMS tests." This yielded a sensitivity and specificity of 94% and 86%, respectively. Further, the authors investigated the relationship between BICAMS performance and self-reported vocational status. The likelihood of vocational disability increased as the number of BICAMS tests yielding impairment increased. A Hungarian translation also demonstrated group differences between MS and control groups at baseline and follow-up with the exception of the CVLT-II at baseline. Cognitive impairment was documented in 52.3% of their sample using the "one or more abnormal tests" criterion. The Hungarian group documented negative correlations between MS participants' subjective fatigue scores and their cognitive performance on the BICAMS. An Italian version was developed and regression-based norms have been established [40]. The Italian BICAMS identified impairment in 23.9% of the MS sample and yielded a sensitivity of 58.2% and a specificity of 86.7% when impairment was defined with Rao's Brief Repeatable Battery [24]. Finally, an Irish version of the BICAMS [41] yielded impairment on one or more tests in 57% of their sample. The MS and control groups differed on all three BICAMS measures when examining mean raw scores. There was no relationship documented between cognitive impairment and fatigue, depression, or anxiety. Similar studies in other countries are ongoing and results are pending.

In summary, there is a need for a short and easily-administered battery of tests that can identify cognitive impairment in an MS clinic setting. Identification of cognitive impairment will help clinic staff identify those in need of cognitive rehabilitation. The BICAMS battery was developed to be suitable for administration by non-specialized personnel and to possess sound psychometric qualities (i.e. reliability, validity). International collaboration is being fostered so that BICAMS may serve as a viable outcome measure of cognition in clinical trials. International standards for validation have been developed and were applied here [37]. The objectives of the current prospective study were to first, establish BICAMS as a feasible cognitive monitoring tool in the Ottawa MS clinic and second, to provide Canadian data toward the international validation effort to foster global collaboration. We hypothesized that PWMS would perform worse than healthy controls (HC) on BICAMS (criterion-related validity) and that BICAMS would demonstrate high test–retest reliability. Secondary considerations were to determine if BICAMS correlated with self-reported cognition and if BICAMS performance predicts vocational status.

2. Method

2.1. Study population

57 English-speaking individuals with clinically definite MS were matched to 51 English-speaking healthy controls (HC) on age, sex and education. Participants with MS were recruited from the Ottawa Hospital MS Clinic, whereas healthy controls were recruited from the community, family/friends of MS participants (no first degree relatives), and through website advertisements. Participants were between the ages of 18 and 59 and fluent in English. They were excluded if they had any neurological/medical/psychiatric conditions (besides MS and depression) that might impede cognition including prior head trauma or a learning disability. Other exclusion criteria included history of seizures, uncorrected visual acuity problems, corticosteroid or immunosuppressive treatment within 2 months of enrolment, current MS exacerbation and current use of drugs (legal or illegal) which may have an impact on cognitive function.

2.2. Procedures

The study was approved by the Ottawa Health Science Network Research Ethics Board. Participants were compensated for their parking costs, but did not receive any incentives for participation. After undergoing appropriate informed consent procedures and a demographic interview, participants underwent the BICAMS battery, which included the oral SDMT (Rao version) as well as the learning trials from the CVLT-II and the BVMT-R (published versions). Tests were administered in that same fixed order. Depression was measured with the Patient Health Questionnaire-9 (PHQ-9) [42]. This is a freely available tool that is quick to administer and has been validated in MS [43,44]. Self-reported cognition was assessed with the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ – informant and self forms), a well validated measure of subjective cognitive deficits that often accompany MS [45]. Fatigue was measured with the Modified Fatigue Impact Scale [46].

Participants were then asked to return for a follow-up session one to three weeks later (mean interval 15.6 (2.0) days; range 9 to 32 days; all numbers between parentheses are standard deviations) to allow for test–retest reliability to be determined. This is the gold standard separation interval when the question is test reliability, controlling for maturation effects. All tests administered in the baseline session were repeated