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Remote Assessment of Verbal Memory in MS Patients Using the California Verbal Learning Test

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Abstract

We utilized the California Verbal Learning Test, Second Edition (CVLT-II), one component of the Brief International Cognitive Assessment for Multiple Sclerosis (MS) (BICAMS), to determine feasibility of a remote assessment protocol. We compared telephone administered CVLT-II data from MS patients to data acquired in person from an independent sample of patients and healthy controls. Mixed factor ANOVAs showed no significant differences between patient groups but between-group effects comparing patients and healthy controls were significant. CVLT-II assessment by conventional in-person and remote telephone assessment yield indistinguishable results. The findings indicate that telephone administered CVLT-II is feasible. Further validation studies are underway.

Keywords

multiple sclerosis; cognitive impairment; CVLT-II

INTRODUCTION

Multiple Sclerosis (MS) symptoms vary greatly, but cognitive impairment may affect 40–70% of patients [1]. Cognitive processing speed (CPS) and episodic memory are most often involved, both having adverse impact on employment and quality of life [2]. Full characterization of cognitive ability in MS requires psychometric assessment of CPS and memory, using tests with established reliability and validity. These tests may be brief, but typically require a one-on-one clinical evaluation with a psychologist or similarly trained

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professional. This approach is not practical for large-scale clinical, genetic or epidemiologic studies, which require an abundance of information to be collected on hundreds or thousands of participants. Thus, an easily administered, inexpensive and sensitive assessment tool that could be given remotely would facilitate large sample studies of cognitive health in MS. Such a test could also facilitate clinical management by early identification of cognitive deficits.

Currently, there is no formally validated test to assess MS cognitive function remotely. Further, feasibility studies involving remote testing of a large number of MS patients have not been attempted. Herein, we investigated a telephone-administered version of the California Verbal Learning Test, Second Edition (CVLT-II) [3], which has already been validated for in-person assessments of individuals with MS [4], and is a performance based objective measure of ability.

SUBJECTS AND METHODS

Study Population

MS cases for remote CVLT-II assessment were recruited from the Kaiser Permanente Medical Care Plan in Northern California Region (KPNC); an integrated health services delivery system with 3.3 million members in a 22-county service area in Northern California. Criteria for participation and recruitment procedures are described in Supplementary Information. Previously recruited MS cases and controls from University at Buffalo (UB) were individually matched by an investigator blind to CVLT-II performance. Matching variables were age, sex and education (all individuals), and for the MS groups, both disease duration and disease course. See Supplementary Information for details. A total of 180 MS cases and 90 controls were studied.

Cognitive Assessment

KPNC MS Research Program participants completed the CVLT-II as a remote telephone assessment with the same trained staff interviewer. Data were recorded electronically. UB participants were assessed in person, for which the standard version of the CVLT-II has been validated. The standard CVLT-II word list was used for both *remote* and *in-person* testing. The CVLT-II comprises a 16-item word list read aloud five times ('CVLT-II Trials 1–5') to the participant in the same order. After each reading the participant recalls as many words as he/she can, in any order. Recall scores for each trial are derived. The assessment typically requires 10 minutes, including instructions, testing and responses. A strict protocol for remote CVLT-II assessment was followed, as described in Supplementary Information.

Statistical Analysis

MS case and control demographic and clinical characteristics were compared using a t-test or chi-square test when appropriate. A three [group] x five [trial] mixed factor ANOVA was used to compare MS case and controls groups, with an interaction effect determining the influence of testing method over time. Pair-wise analyses were also performed to test differences between MS case groups and each MS case group with controls (t-test). Statistical analyses were conducted using SPSS.

RESULTS

A summary of study participants is shown in Table 1; a total of 270 individuals were studied. No differences were observed for any clinical and demographic characteristics among study subjects. We compared CVLT-II data for KPNC MS cases collected remotely to data collected for the independent sample of both UB MS cases and controls using standard, validated in-person procedures.

Results derived from mixed factor ANOVA for the three groups and five trials are shown in Figure 1. Overall, the observed time and group effects were significant ($p < 0.001$). Both MS case groups were compared separately to controls. CVLT-II results for both remotely and in-person assessed MS cases were significantly different from the in-person assessed controls ($p < 0.0001$). We repeated the analysis for remotely and in-person assessed MS case groups. No differences between MS case groups were detected ($p > 0.50$); no interaction between group and trial was observed for any comparison ($p > 0.10$).

DISCUSSION

Cognitive impairment is common in MS and has important prognostic implications. However, in most centers, neuropsychological assessment is not routinely performed at clinical appointments due to time, cost and infrequent visits for some patients. Our results indicate data collected through remote and standard, validated in-person administration of the CVLT-II yield very similar results for MS groups matched on demographic and disease quality variables. Further, remotely assessed MS cases were distinguished from in-person assessed controls, similar to results observed for the in-person assessed MS cases.

There is a wealth of literature supporting the validity of the CVLT-II in MS, hence its inclusion in the Minimal Assessment of Cognitive Function in MS (MACFIMS) [5] and BICAMS [4]. The CVLT-II is reliable [6], predicts employment status [7], is responsive to treatment [8], and is robustly correlated with brain MRI measures of lesion volume and gray matter volume loss [1, 2]. Despite the utility of the CVLT-II, technician time for testing in the clinic, cost and patient accessibility are major challenges. By assessing memory in patients prior to a clinic visit, using this telephone or other web-based approaches, we may be able to meet the goal of routine neurocognitive monitoring of MS patients, as recently suggested [9].

Our work represents an initial effort to address this problem by measuring verbal memory remotely. We have carefully followed the CVLT-II protocol and find that not only do our data match an in-person assessment, the approach is feasible. Our preliminary experience with the web-supported telephone CVLT-II suggests that we are able to identify individuals with early significant cognitive impairment who are at increased risk of job loss and more rapid disease progression. MS clinic staff may be alerted prior to patient visits. Remote cognitive monitoring as described here can also facilitate large, systematic and longitudinal studies which are needed to identify risk factors for this important clinical outcome. Individuals with MS who are at greatest risk for cognitive impairment or who present with

cognitive impairment could be targeted for intervention strategies to improve or restore cognitive function.

Our results show that in MS, CVLT-II administered remotely yields scores statistically indistinguishable from an independent group taking the test in the traditional manner. Further, both MS groups underperform relative to healthy controls, regardless of administration. However, more thorough validation research is needed, and is in progress. Specifically, work in progress using a counter-balanced design will compare in-person and remote CVLT-II testing in 100 MS patients. In addition, more work is needed to test with greater certainty that potential sources of testing error are not compromising CVLT-II validity. For example, patients could get assistance from a family member, be distracted by the surrounding environment, and/or record test words during the assessment rather than recalling them from memory. To reduce this possibility, several important safeguards were in place as part of our protocol (Supplementary Information) but additional work is needed to insure that these safeguards are effective. There may be individual patients for whom phone administration is not feasible; however, this possibility was not cited by patients invited to the current study as a reason for refusing to participate. We do believe that this form of testing is feasible. Recently, we performed computer assisted telephone interviews of more than 2,600 individuals (half were MS patients) that included the Modified Telephone Interview for Cognitive Status (TICS-M), a validated phone assessment to detect mild cognitive impairment in healthy elderly populations [10]. We identified factors that influenced participation; feasibility of phone administration was not among them. Finally, the administration of CVLT-II only included the immediate recall portion of the task, not the interference or delayed recall portions. Therefore, we were not able to evaluate the equivalence of those aspects of task performance. We plan to include these additional assessments in our remote protocol for future studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Comparison of standard, in-person CVLT-II results from an independent sample of MS cases and controls with a sample of remotely assessed MS cases

Results show CVLT-II data collected from MS cases using standard in-person and remote protocols are very similar, and can be distinguished from control data (in-person); five trials were performed; Y-axis shows mean score range for the CVLT-II. Mean raw scores are plotted with standard error bars.

Table 1

Characteristics of Kaiser Permanente Northern California Region (KPNC) MS Cases and University of Buffalo (UB) Cases and Controls

	KPNC Patients Mean (SD) or Frequency (%)	UB Patients Mean (SD) or Frequency (%)	UB Controls Mean (SD) or Frequency (%)
Number of individuals (N)	90	90	90
Age at assessment (years)	49.6 (9.4)	51.7 (9.3)	50.3 (7.3)
Sex (Female) (N, %)	71 (79%)	71 (79%)	71 (79%)
Disease subtype (N, %) (RR and SPMS)	78 (87%)	81 (90%)	-
Education (years)	15.5 (2.4)	15.2 (2.8)	15.1 (2.4)
Race/Ethnicity (White, non-Hispanic/Black/Other)	84/5/1	84/5/1	79/10/1
Disease duration (years)	16.1 (9.3)	16.9 (9.8)	-

Abbreviations used: SD = standard deviation, RRMS = relapsing remitting MS, SPMS = secondary progressive MS; Student's T-test was used to compare continuous variables between cases and controls; a chi-square statistic was used to compare categorical variables.