Initial Evaluation of *MSCogScreen*: A Multi-Domain, MS-Specific Digital Cognitive Screening Tool

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Introduction

- Annual cognitive screenings are a recommended component of MS care, but they are not routinely done [1,2].
- Digital options, such as tablet-based tests, may be easier to integrate into clinics due to their increased portability and automated scoring options [3].
  - However, few of these screening tools assess elements beyond information processing speed, and even fewer have been co-developed with people living with MS [3].

Objectives/Aims

- To evaluate the validity, level of difficulty (interform parallelism), and scoring consistency between different raters (interrater reliability) on the three versions of *MSCogScreen*, a new MS-specific cognitive screening battery.

Methods

Participants:

- People with MS (n = 56) completed a brief reference battery [4-7] and all three versions of *MSCogScreen* during a one-time visit.
  - Randomized into one of four testing orders to control for practice effects.
- Demographics:
  - *Age (median)*: 58 (26-79)
  - *Gender*: 73.2% women
  - *Education*: 60.7% with ≥ 16 years
  - *Race/Ethnicity*: 67.9% White non-Hispanic
  - *MS Subtype*: 80.4% relapsing remitting MS
  - *Impaired on the BICAMS* [8]: 75.0%

Measures:

- *MSCogScreen*: each version has six subtests with novel stimuli.
  - Prospective Memory (PM): verbal response after 15-minute delay.
    - Delay filled by other tests and several patient-reported outcome measures.
  - Verbal Learning (VL): two learning trials of 15 non-semantically clustered words.
  - Visuospatial Learning (VSL): two learning trials of 3x2 grid of geometric designs.
  - Letter Fluency (LF): one letter with 60-second response time.
  - Semantic Fluency (SF): one category with 60-second response time.
  - Processing Speed (PS): verbal matching of numbers to symbols with 30-second response time.

Procedures:

- A 10th generation iPad was used to administer *MSCogScreen*.
  - Figma, a web-based tool for designing and testing prototypes, was used to display patient-facing screens, with conditional logic to mimic responsive functionality.
  - Verbal responses were recorded with an external microphone.
  - Drawings were collected using Adobe Fresco on the same iPad.

Statistical Analyses:

- *Convergent validity*: partial correlations controlling for testing order.
- *Interform parallelism*: repeated measures ANOVA controlling for testing order.
  - Both analyses were conducted using the full sample and then repeated after removing outlier performances.
    - Based on observations during testing and confirmed using scatterplots.
- *Interrater reliability*: two-way mixed effects, absolute agreement, single-measure intraclass correlation coefficients (ICCs).

Results

MSCogScreen	Reference Battery Measures					
	PM	VL	VSL	LF	SF	PS
Form 1	0.57 (0.70[a])	0.63 (0.68[b])	0.73 (0.78[c])	0.68 (0.73[c])	0.47 (0.67[d])	0.85 (0.87[e])
Form 2	0.44 (0.63[a])	0.67 (0.67[b])	0.71 (0.79[c])	0.71 (0.70[c])	0.42 (0.62[d])	0.85 (0.83[e])
Form 3	0.57 (0.70[a])	0.71 (0.73[b])	0.72 (0.79[c])	0.66 (0.78[c])	0.62 (0.74[d])	0.85 (0.86[e])

Table 1: Correlations between *MSCogScreen* subtests and their respective reference battery measure, controlling for testing order. Results with outliers removed are in parentheses.
[a] n = 48; [b] n = 54; [c] n = 52; [d] n = 44; [e] n = 53

MSCogScreen	PM		VL		VSL	
	Mean Difference	*p*-value	Mean Difference	*p*-value	Mean Difference	*p*-value
Form 1 - Form 2	-0.08 (-0.13[a])	>.999 (.450[a])	-0.14 (-0.15[b])	>.999 (>.999[b])	-0.69 (-0.70[c])	>.999 (>.999[c])
Form 1 - Form 3	-0.01 (-0.02[a])	>.999 (>.999[a])	-0.13 (-0.06[b])	>.999 (>.999[b])	-1.21 (-1.17[c])	.680 (.805[c])
Form 2 - Form 3	0.07 (0.10[a])	>.999 (.953[a])	0.02 (0.09[b])	>.999 (>.999[b])	-0.52 (-0.47[c])	>.999 (>.999[c])

Table 2: Bonferroni-corrected pairwise comparisons between the different versions of *MSCogScreen* subtests. Results with outliers removed are in parentheses.
[a] n = 48; [b] n = 54; [c] n = 52

MSCogScreen	LF		SF		PS	
	Mean Difference	*p*-value	Mean Difference	*p*-value	Mean Difference	*p*-value
Form 1 - Form 2	1.43 (1.10[a])	.004 (.036[a])	2.84 (2.14[b])	.001 (.001[b])	-0.11 (-0.09[c])	>.999 (>.999[c])
Form 1 - Form 3	-0.61 (-0.44[a])	.383 (.754[a])	4.29 (3.25[b])	<.001 (<.001[b])	-0.14 (-0.34[c])	>.999 (>.999[c])
Form 2 - Form 3	-2.04 (-1.54[a])	<.001 (<.001[a])	1.45 (1.11[b])	.103 (.113[b])	-0.04 (-0.25[c])	>.999 (>.999[c])

Table 3: Bonferroni-corrected pairwise comparisons between the different versions of *MSCogScreen* subtests. Results with outliers removed are in parentheses.
[a] n = 52; [b] n = 44; [c] n = 53

MSCogScreen	PM	VL	VSL	LF	SF	PS
Form 1	0.96 (0.94, 0.98)	0.97 (0.91, 0.99)	0.87 (0.73, 0.93)	0.96 (0.88, 0.98)	0.99 (0.98, 0.99)	1.00 (0.99, 1.00)
Form 2	0.97 (0.95, 0.98)	0.96 (0.88, 0.98)	0.87 (0.77, 0.92)	0.98 (0.91, 0.99)	0.97 (0.95, 0.98)	1.00 (0.99, 1.00)
Form 3	0.96 (0.94, 0.98)	0.96 (0.88, 0.98)	0.85 (0.63, 0.93)	0.95 (0.85, 0.98)	0.98 (0.95, 0.99)	1.00 (1.00, 1.00)

Table 4: ICCs (95% CI) between two independent raters on *MSCogScreen* subtests.

Conclusions

- Early evidence suggests that *MSCogScreen* may be a viable cognitive screening tool for people with MS.
  - *MSCogScreen* can be completed in a similar amount of time as the BICAMS (14.10 ± 2.17 minutes), with the PS subtest taking only 1.75 minutes.
  - VL, VSL, LF, and PS subtests had good convergent validity, interform parallelism, and interrater reliability.
  - LF also had good convergent validity and interrater reliability, with one version (Form 2) being slightly harder.
    - Next iteration will include adjustments to the instructions. If significant differences remain, a point correction will be considered.
- As PM and SF subtests had a high number of outliers, the following changes have been proposed:
  - PM: change to an optional test, where it would be used as a flag for further evaluation of this domain and not included in the impairment calculation.
    - Decreases battery completion time to 11.33 ± 1.51 minutes.
  - SF: several changes to instructions, including having patient repeat back the category they are doing (like LF) and adjusting the category presentation for Forms 2 and 3.
    - Will then reevaluate SF's psychometric properties.

Acknowledgments

This study was funded by a pilot grant from the Consortium of MS Centers and a William P. Haas Research Development Award from St. Francis Hospital and Medical Center. Dr. Gromisch is a Harry Weaver Scholar of the National MS Society.

Jill Blewitt also contributed to this study as a Patient Advisor.

The views and opinions expressed in this article reflect those of the authors and do not necessarily reflect those of the United States Department of Veterans Affairs.

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Disclosures

Dr. Gromisch has received funding from the Consortium of MS Centers and the National MS Society. Dr. Imitola has received funding from the National MS Society, National Institutes of Health, and Genetech. Dr. DeLuca has received funding from Biogen, EMD Serono, Roche, Bristol Myers Squibb, National MS Society, Consortium of MS Centers, National Institutes of Health, and MS Society of Canada. Dr. DeLuca has also served on an Advisory Board for Biogen, Novartis, Celgene/Bristol Myers Squibb, Roche, Janssen, and MedRhythms; a consultant for Celgene/Bristol Myers Squibb, Sanofi-Genzyme, and Centessa; and on a speakers bureau for Biogen. Dr. Turner, Ms. Neto, Ms. Harbajan, Dr. Raskin, Dr. Foley, Dr. Zemon, Mr. Doiron, Ms. Sindoni, Ms. Souss, Dr. Gokhale, and Dr. Agresta have nothing to disclose.