

MS Center Amsterdam

Introducing Multiple Screener: An unsupervised digital screening tool for cognitive deficits in MS

L. van Dongen¹, B. Westerik¹, K. van der Hiele², L.H. Visser^{3,4}, M.M. Schoonheim¹, L. Douw¹, J.W.R. Twisk⁵, B.A. de Jong⁶, J.J.G. Geurts¹, H.E. Hulst¹

¹Amsterdam UMC, Vrije Universiteit Amsterdam, department of Anatomy & Neurosciences, Amsterdam Neuroscience, VUmc MS Center Amsterdam, de Boelelaan 1117, Amsterdam; ²Department of Psychology, Health, Medical and Neuropsychology Unit, Leiden University, Leiden; ³Department of Neurology, Elisabeth-Tweesteden Hospital, Tilburg; ⁴Department of Care Ethics, University of Humanistic Studies, Utrecht; ⁵Amsterdam UMC, Vrije Universiteit Amsterdam, department of Epidemiology and Biostatistics, de Boelelaan 1117, Amsterdam; ⁶Amsterdam UMC, Vrije Universiteit Amsterdam, department of Neurology, Amsterdam Neuroscience, VUmc MS Center Amsterdam, de Boelelaan 1117, Amsterdam; the Netherlands

BACKGROUND Cognitive deficits affect up to 70% of all patients with MS and have a significant impact on quality of life [1-3]. **Neuropsychological testing is necessary for timely identification and monitoring of cognitive decline over time.** Brief test batteries, such as the Brief International Cognitive Assessment for MS (BICAMS) [4,5], exist. However, **the paper-and-pencil based BICAMS needs to be administered by a test leader, making it still too time-consuming to implement in standard routine clinical care.**

OBJECTIVE To develop a time-efficient, unsupervised, digital, screening tool for cognitive deficits in patients with MS: **Multiple Screener.**

METHODS

Multiple Screener consists of two segments.

- Psychological:** well being (anxiety, depression, fatigue) is assessed.
- Cognitive:** neuropsychological tests are based on the BICAMS: (1) SDMT, (2) Dutch version of the CVLT-II, and (3) SPART (instead of the Brief Visuospatial Memory Test-Revised (BVMT-R), since a digital version of the BVMT-R was too difficult to score automatically).

Part 2.1. Clarity and feasibility

Qualitative evaluation of the Multiple Screener tool (questionnaire)

16 patients with MS

mean age 50.9 years (SD 9.4, range 37-68)

Part 2.2. Comparison between paper and digital assessment

Intraclass correlation coefficients (ICC)

60 healthy controls (HCs)

mean age 44.5 years (SD 14.0, range 18-67)

Part 2.3. Norm data

Step 1: Multiple linear regression - effects of age, sex, and educational level

Step 2: Regression-based correction for age-effect on the raw test scores

Step 3: If necessary, additional correction for sex or educational level (calculated per bin (men and women; high and low educational level))

236 HCs

mean age 42.8 years (SD 12.8, range 18-69)

CONCLUSION

- The clarity and feasibility of the Multiple Screener tool was confirmed.
- Performance on the adjusted, digital version of the BICAMS correlated well with the standard paper-and-pencil based test scores in HCs.
- Multiple Screener is an unsupervised, digital, screening tool, with available norm scores, and together with the online assessment of confounders (anxiety, depression, fatigue [6]), it is a promising tool to **timely identify and easily monitor cognitive decline in patients with MS.**

FUTURE PERSPECTIVES

- Validate the tool (sensitivity and specificity) in patients with MS
- Determine optimal clinical cut-off scores

REFERENCES

1. Rao, S.M., et al., Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. *Neurology*, 1991. 41(5): p. 685-91. 2. Chiaravalloti, N.D. and J. DeLuca, Cognitive impairment in multiple sclerosis. *Lancet Neurol*, 2008. 7(12): p. 1139-51. 3. Van der Hiele, K., et al., A pilot study on factors involved with work participation in the early stages of multiple sclerosis. *PLoS One*, 2014. 9(8): p. e105673. 4. Langdon, D.W., et al., Recommendations for a Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS). *Mult Scler*, 2012. 18(6): p. 891-8. 5. Benedict, R.H., et al., Brief International Cognitive Assessment for MS (BICAMS): international standards for validation. *BMC Neurol*, 2012. 12: p. 55. 6. Boeschoten, R.E., et al., Prevalence of depression and anxiety in Multiple Sclerosis: A systematic review and meta-analysis. *J Neurol Sci*, 2017. 372: p. 331-341.

DISCLOSURES

L. van Dongen, B. Westerik, and J.W.R. Twisk have nothing to disclose. K. van der Hiele received honoraria for consultancies, presentations and advisory boards from Sanofi Genzyme and Merck-Serono. L.H. Visser received honoraria for lectures, grants for research and honoraria for advisory boards from Sanofi Genzyme, Merck-Serono, Novartis and Teva. M.M. Schoonheim serves on the editorial board of *Frontiers of Neurology*, receives research support from the Dutch MS Research Foundation, grant number 13-820, and has received compensation for consulting services or speaker honoraria from ExCeMed, Genzyme and Biogen. L. Douw receives research support from Society in Science (Branco Weiss Fellowship). B.A. de Jong has received speaker and consulting fees from Merck-Serono, Biogen, TEVA, Genzyme and Novartis. J.J.G. Geurts is an editor of *MS journal* and serves on the editorial boards of *Neurology* and *Frontiers of Neurology* and is president of the Netherlands organization for health research and innovation and has served as a consultant for Merck-Serono, Biogen, Novartis, Genzyme and Teva Pharmaceuticals. H.E. Hulst receives research support from the Dutch MS Research Foundation, grant number 12-548, and has received compensation for consulting services or speaker honoraria from Sanofi Genzyme, Merck-Serono and Biogen Idec.

RESULTS

Table 1. ICCs with 95% confidence intervals (CI)

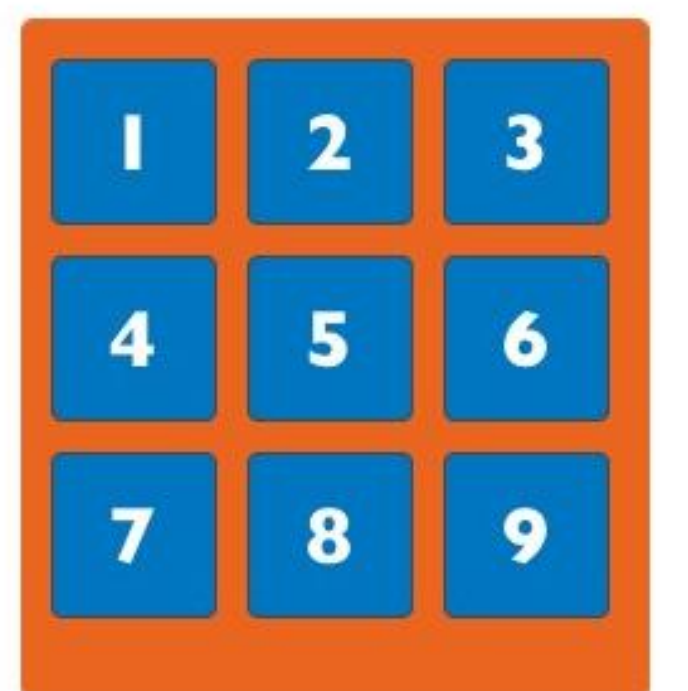
Test	ICC	CI
SDMT	0.79	0.67-0.87
CVLT-II	0.77	0.64-0.85
SPART	0.61	0.42-0.75

Two-way mixed effects model, relative agreement, single rater

1. Symbol Digit Modalities Test (SDMT) - information processing speed

+	>	-	÷	+	Γ	>	÷	+	+
1	2	3	4	5	6	7	8	9	

+	-	+	+	+	+	+	+	+	+
5	6	5	5	2	1	2	6	1	2
+	>	+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+	+	+



2. California Verbal Learning Test (CVLT-II) - verbal memory (Dutch version)



3. Spatial Recall Test (SPART) - visuospatial memory

