Konectom™ Cognitive Processing Speed Testing and the Influence of Reaction Time

Scaramozza M,[1] Chiesa PA,[1] Scotland A,[1] Sun Z,[1] Rajbhandari R,[1]* Juraver A,[1] Brochet B,[2] Deloire M,[2] Charre-Morin J,[2] Dulong C,[3] Shen C,[1] Carment L,[3] Guymard T,[1] van Beek J,[1] Ruiz M,[1] Belachew S,[1] Ruet A[2]

[1]Biogen, Cambridge, MA, USA; [2]Centre Hospitalier Universitaire Bordeaux, Bordeaux, France; [3]Ad Scientiam, Paris, France

*Employee of Biogen at the time this study was conducted

OBJECTIVE

- To explore the reliability and convergent validity of Konectom smartphone-based cognitive processing speed test reaction time features against standard measures of cognition and disability in people with multiple sclerosis (PwMS).

CONCLUSIONS

- Cognitive processing speed can reliably be self-assessed remotely by PwMS using Konectom.
- Konectom CPS Test reaction time features correlated with Symbol Digit Modalities Test and Expanded Disability Status Scale.
- Use of Konectom reaction time digital features to assess information processing speed should be further explored. Potential nonredundancy between symbol-to-digit reaction time and digit-to-digit reaction time will be further elucidated using additional intra-test digital features between respective tests.

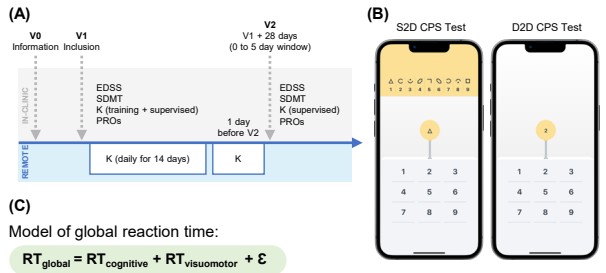
Introduction

- Symbol Digit Modalities Test (SDMT) is a standard clinical assessment in multiple sclerosis (MS) trials but requires in-clinic administration and may not capture the full extent of cognitive decline experienced by people with MS (PwMS).[1]
- Reaction time has been shown to predict cognitive performance in disease settings.[2,3]
- Smartphone-based Konectom cognitive processing speed (CPS) test is designed to measure information-processing speed in free-living environments while accounting for visuomotor reaction time.
  - Konectom includes the traditional symbol-to-digit (S2D) substitution task followed by a digit-to-digit (D2D) matching test to isolate the visuomotor component of the CPS Test.
  - Capturing S2D reaction time while subtracting the D2D reaction time provides a digital outcome assessment of cognitive processing speed independent of the information processing time associated with visuomotor reactivity.
  - The separate assessment of D2D reaction time is a novel digital feature of the Konectom CPS Test that requires simple digit matching and reflects visuomotor function. D2D reaction time could represent a secondary test feature to detect subtle impairment in PwMS.

Methods

- The DigiToms study (NCT04756700) includes people with multiple sclerosis (PwMS) aged 18–64 years with an Expanded Disability Status Scale (EDSS) score ≤ 6.0.
- Baseline in-clinic assessments included Konectom CPS Test, EDSS, and SDMT.
  - Overall study design is presented in Figure 1A, and additional details on Konectom are presented in poster P50.
- Konectom CPS Test was to be self-administered remotely during a period of 14 consecutive days to assess its clinical validity and reliability.
  - Konectom CPS substitution time was derived by subtracting mean D2D reaction time from mean S2D reaction time for correct responses for each test (Figure 1B and C).
- Relationship between conventional in-clinic measures (SDMT, EDSS) and CPS Test was assessed using Spearman's rank correlation and Pearson's correlation coefficient.

Figure 1. (A) Overall DigiToms Study Design, **(B)** Screenshots of Konectom CPS Test Showing S2D Substitution and D2D Matching Tests, and **(C)** Derivation of CPS Substitution Time



(C)

Model of global reaction time:

$$RT_{global} = RT_{cognitive} + RT_{visuomotor} + \varepsilon$$

Deriving CPS ST:

CPS ST = S2D reaction time – D2D reaction time

CPS ST = Cognitive Processing Speed Substitution Time; CPS = cognitive processing speed; D2D = digit-to-digit; EDSS = Expanded Disability Status Scale; K = Konectom app test; PRO = patient-reported outcome; RT = reaction time; S2D = symbol-to-digit; SDMT = symbol digit modalities test; V = visit

Results

- At the interim data cut (18 August 2021), 40 PwMS had completed the study.
  - Mean (SD) age was 41.9 (9.4) years, and 82.5% of PwMS were female (Table 1).
  - Median (interquartile range) EDSS score was 2.0 (1.5).
- Remote test-retest reliability (intraclass correlation coefficient) for CPS substitution time testing was good (0.74).

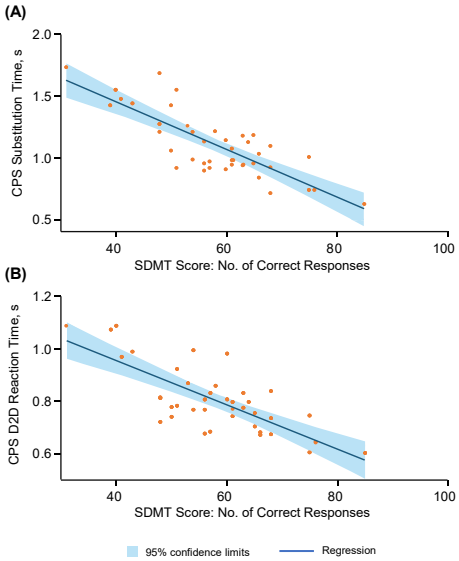
Table 1. Patient Demographics and Baseline Characteristics

Variable	Interim Study Population (N = 40)
Age, y, mean (SD)	41.9 (9.4)
Female, n (%)	33 (82.5)
Educational level, n (%)	
No A-Level/High School Diploma	5 (12.5)
A-Level/High School Diploma	8 (20.0)
Bachelors Degree	19 (47.5)
Masters Degree or higher	8 (20.0)
Disease duration, y, mean (SD)	11.4 (8.5)
EDSS score, median (IQR)	2 (1.5)
Disease subtype, n (%)	
Relapsing-remitting MS	38 (95.0)
Secondary progressive MS	2 (5.0)
Number of relapses in prior 12 months, median (IQR)	0 (0)
SDMT score, mean (SD)	57.8 (11.1)

EDSS = Expanded Disability Status Scale; IQR = interquartile range; MS = multiple sclerosis; SDMT = Symbol Digit Modalities Test

- There were significant correlations between CPS substitution time and SDMT score (Spearman: ρ = –0.72, p < 0.0001; Pearson: r = –0.81, p < 0.0001; Figure 2A) and between CPS D2D reaction time and SDMT score (Spearman: ρ = –0.65, p < 0.0001; Pearson: r = –0.75, p < 0.001; Figure 2B).

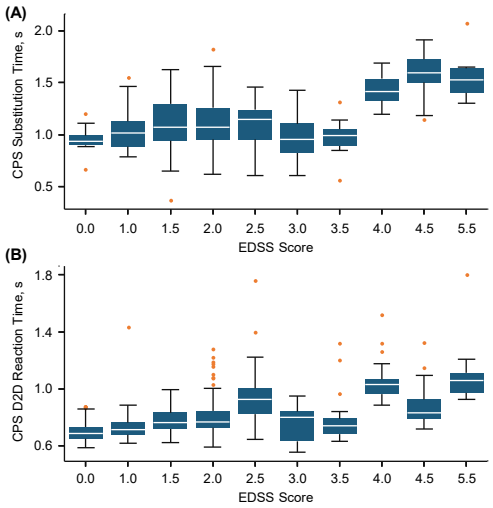
Figure 2. Plots Showing Correlations Between **(A)** CPS Substitution Time and SDMT Score and **(B)** CPS D2D Reaction Time and SDMT Score



CPS = cognitive processing speed; D2D = digit-to-digit; SDMT = symbol digit modalities test

- Moderate correlations were observed between CPS substitution time and EDSS score (Spearman: ρ = 0.41, p < 0.0001; Pearson: r = 0.5, p < 0.0001; Figure 3A) and between CPS D2D reaction time and EDSS score (Spearman: ρ = 0.48, p < 0.0001; Pearson: r = 0.46, p < 0.0001; Figure 3B).
- For the comparison between SDMT score and EDSS score, correlation coefficients were: Spearman, ρ = -0.28 (p = 0.08); and Pearson, r = -0.41 (p < 0.01).

Figure 3. Box Plots Showing Correlations Between **(A)** CPS Substitution Time and EDSS Score and **(B)** CPS D2D Reaction Time and EDSS Score



CPS = cognitive processing speed; D2D = digit-to-digit; EDSS = Expanded Disability Status Scale

References 1. Koch MW, et al. *Eur J Neurol*. 2021;28(6):2115-2120. 2. Jakobsen LH, et al. *Nutrition*. 2011;27(5):561-570. 3. Christ BU, et al. *Front Hum Neurosci*. 2018;12:124.
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