Training effects in smartphone-based tests of cognition, dexterity and mobility in people with multiple sclerosis

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Background

Smartphones and their inbuilt sensors allow for the collection of a wealth of data about their owners.

While passively collected data such as step counts can already provide meaningful insights, active tests allow for measuring function in specific tasks.

Taking advantage of these capabilities could improve disease characterization and monitoring and could potentially support treatment decisions in multiple sclerosis (MS), a multifaceted and variable chronic autoimmune neurological disease.[1-3]

In this study, we set out to identify and compare training effects in active tests for cognition, dexterity and mobility.

Methods

We are using publicly available data from the "Floodlight Open" study, which is collecting smartphone-based test data from self-declared MS patients (feasibility study: NCT02952911).[4]

Recruitment started 04/2018, thus some patients have more than 30 months of data. Data up to January 10 2021 are included.

Inclusion criteria: participation for at least 5 weeks and at least 5 repetitions performed per test, leading to the analysis of

- n=220 / 1003 patients and 3715 / 4918 tests (76%) for cognition (max. one repetition per week)
- n=223 / 973 patients, 418 / 1669 hands and 15284 / 17864 tests (86%) for dexterity (up to daily)
- n=141/483 patients and 10812/11732 tests (92%) for mobility (up to daily)

Bounded growth models are used to estimate average baseline and boundary (asymptote) performances by modelling them as random effects for each patient.

The training effect size is defined as the difference of *asymptote* and *baseline* and the *half-training point* is reached at half the training effect.

Linear quantile regression is used to compare low-performers and high-performers in the time up to the *half-training point* with near-linear growth.

Results

Cognition: Matching symbols

This test is a digital adaptation of the classic symbol digit modality test (SDMT) for information processing speed: patients have to match symbols to digits with a random key as quickly as possible in 90 seconds.

Strong training effects are found with on average 28.6% improvement over baseline (95% CI 28.5%-29.0%), reaching 50% of the training effect at week 9 and 90% at week 28 (Fig. 1A).

Quantile regression slopes of the near linear training phase up to week 9 are near to one additional correct response per week and range from 0.8 at 25th percentile to 1.3 at 5th percentile.

The ANOVA for all 5 slopes being insignificant (p=0.2) suggests that training speeds for low performers (5th and 25th percentile) are similar to those of high performers (75th and 95th percentile), Figure 1B.

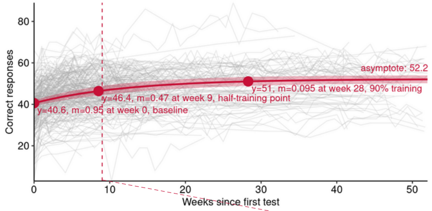

Figure 1A: Cognition, bounded growth model
n tests = 3715 (n patients = 220, median tests per patient: 11, IQR 7-19)

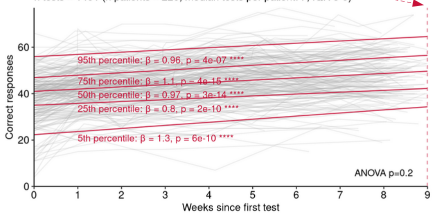

Figure 1B: Quantile regression
n tests = 1491 (n patients = 220, median tests per patient: 7, IQR 5-9)

Dexterity: Finger pinching

Patients have to pinch the screen with two fingers at changing random positions for 60s in this test called "Squeeze a Tomato", which is a digital adaptation of the classic 9-hole-peg-test.

Strong training effects are found with on average 50.52% improvement over baseline (95% CI 50.53%-50.67%). Relative training speed is nearly equal to that of cognition, reaching 50% of the training effect at week 9 and 90% at week 29 (Figure 2A).

Quantile regression slopes of the near linear training phase up to week 9 are on median 1.9 additional successful pinches per week and range from 1.0 at 95th percentile to 1.9 at median.

The ANOVA for all 5 slopes is highly significant (p<0.0001) and suggests faster training speeds for median performers than for low / high performers (Figure 2B).

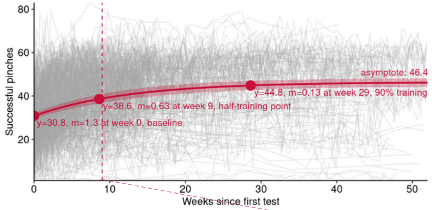

Figure 2A: Dexterity, bounded growth model
n tests = 15284 (n hands = 418, median tests per hand: 19, IQR 10-45)

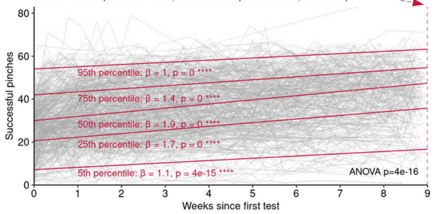

Figure 2B: Quantile regression
n tests = 6448 (n hands = 418, median tests per hand: 13, IQR 7-24)

Mobility: Steps (2min walking)

Patients walk as evenly as possible on level ground for 2 minutes in this test and the total number of steps is considered as outcome.

No relevant training effects are found on the group level with on average 1% improvement over baseline (95% CI 0.9%-1.2%), Figure 3A.

Quantile regression slopes for the first 9 weeks (in order to match the timeframe chosen for cognition and dexterity) only indicate significant training effects for low performers in the 5th and 25th percentiles, not for median and high performers (Figure 3B).

Whether these significant training effects for low performers are due to actual functional improvement cannot be determined without comparative clinical tests.

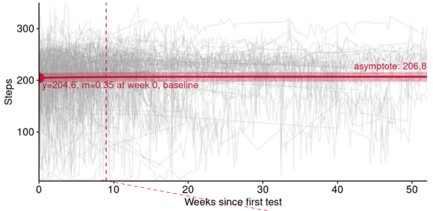

Figure 3A: Mobility, bounded growth model
n tests = 10812 (n patients = 141, median tests per patient: 42, IQR 16-94)

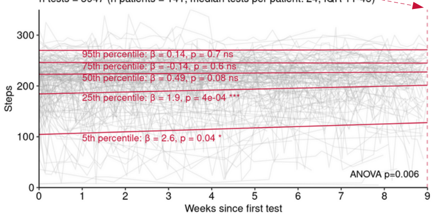

Figure 3B: Quantile regression
n tests = 3947 (n patients = 141, median tests per patient: 24, IQR 11-45)

Conclusions

Smartphone-based tests promise to help monitor MS disease trajectories and there are currently multiple projects in development.[4-6]

Our results suggest that strong training effects in cognitive and dexterity functions have to be accounted for in order to identify possible disease-related changes in these domains, lasting for more than 6 months on average.

On the other hand, the lack of training effects in mobility tests simplifies their interpretation.

Patients in this study are self-declared and there is no confirmation or assessment by health professionals. Variation caused by disease severity and treatment cannot be analysed.

Thus, longitudinal studies with parallel state of the art assessment of traditional outcome measures are needed in order to validate these smartphone-based tests as future digital biomarkers.

References: 1. Bove R et al. *Neurol Neuroimmunol Neuroinflamm* 2015, doi:10.1212/NXI.0000000000000162, 2. Montalban X et al. *Neurology* 2019; 92 (15 Supplement), 3. Midaglia L et al. *JMIR* 2019, doi:10.2196/14863, 4. van Beek et al. *Annual Meeting of the CMSC* 2019, 5. Guo C et al. *MSVirtual* 2020, P0102, 6. Naegelin Y et al. *MSVirtual* 2020, P0069, doi:10.13140/RG.2.2.23703.19362,