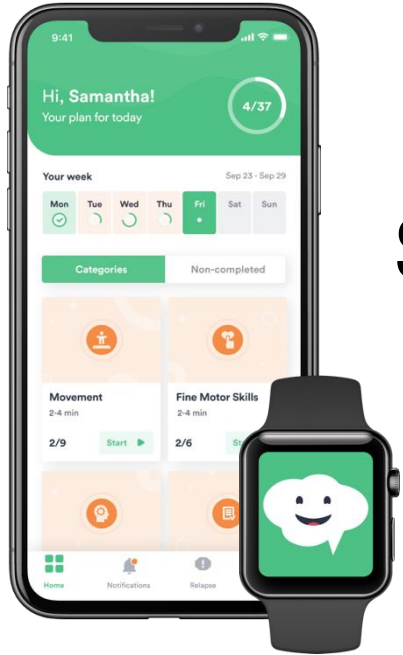
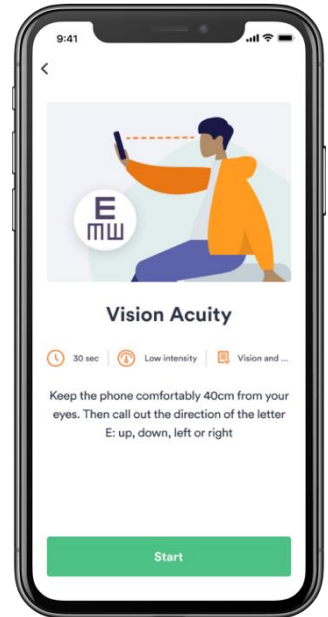




Smartphone-Based Digital Biomarkers in Multiple Sclerosis and Their Learning and Practice Effects

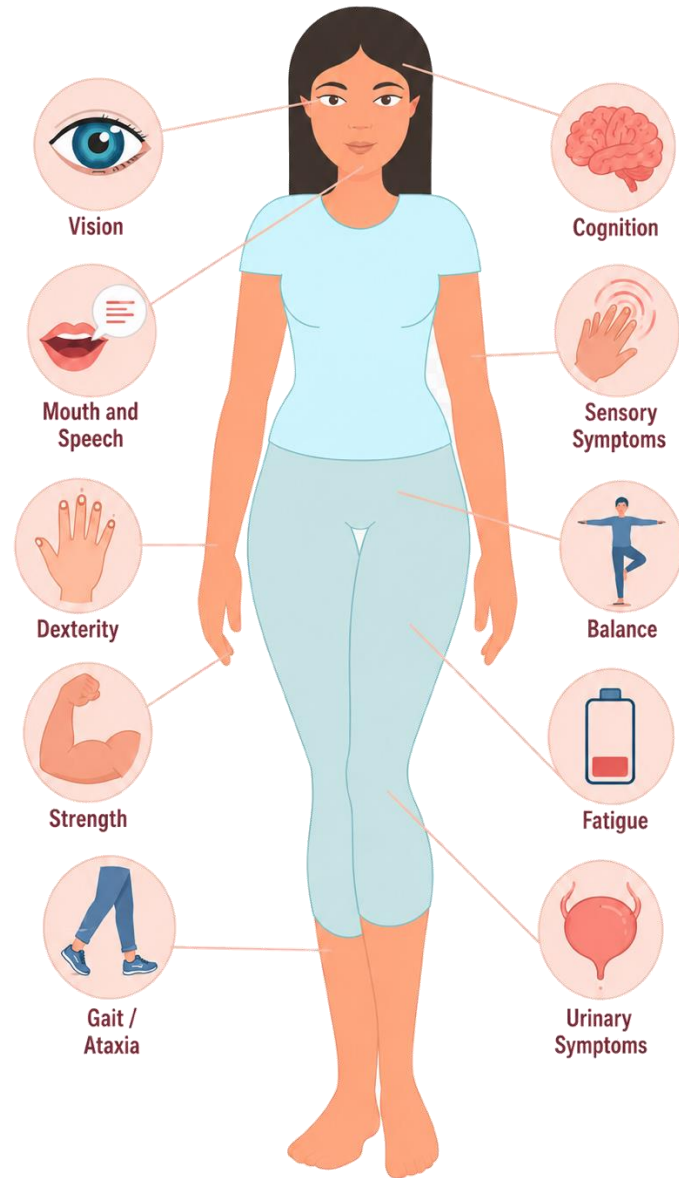
Dr. med. Tim Woelfle, 27.08.2026



Disclosures

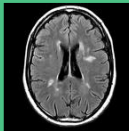
- My institution RC2NB received speaking honoraria from Merck
- My institution RC2NB is funded by Innosuisse, Novartis, Roche, among others
- The dreaMS app is developed by our industry partner Indivi AG

Multiple Sclerosis



Why do we need to measure MS?

- How is the course of the disease?
- Are there relapses or is there disease progression?
- Which medication is optimal for each MS patient?
- Digital endpoints for interventional studies (e.g. new therapies)

Januar	Februar	März	April	Mai	Juni	Juli	August	September	Oktober	November	Dezember
1 Fr Neujahr	1 Mo ⁰⁵	1 Mo ⁰⁹	1 Do	1 Sa Tag der Arbeit	1 Di	1 Do	1 So	1 Mi	1 Fr	1 Mo	1 Mi
2 Sa	2 Di	2 Di	2 Fr Karfreitag	2 So	2 Mi	2 Fr	2 Mo ³¹	2 Do	2 Sa	2 Di	2 Do
3 So	3 Mi	3 Mi	3 Sa	3 Mo ¹⁸	3 Do	3 Sa	3 Di	3 Fr	3 So Tag der Dt. Einheit	3 Mi	3 Fr
4 Mo ⁰¹	4 Do		4 So	4 Di	4 Fr	4 So	4 Mi	4 Sa	4 Mo ⁴⁰	4 Do	4 Sa
5 Di	5 Fr		5 Mo Ostermontag ¹⁴	5 Do	5 Sa	5 Mo ²⁷	5 Do	5 So	5 Di	5 Fr	5 So
6 Mi Heilige 3 Könige	6 Sa		6 Di	6 So	6 So	6 Di	6 Fr	6 Mo	6 Mi	6 Sa	6 Mo ⁴⁹
7 Do	7 So		7 Mi	7 Mo ²³	7 Mo ²³	7 Mi	7 Di	7 Di	7 Do	7 So	7 So
8 Mo	8 Mo ⁰⁶	8 Mo Int. Frauentag	8 Do	8 Sa	8 Do	8 Do	8 Mi	8 Mi	8 Fr	8 Mo ⁴⁵	8 So
9 Di	9 Di		9 Fr	9 So	9 Mi	9 Fr	9 So	9 Do	9 Sa	9 Di	9 Di
10 Mi	10 Mi		10 Sa	10 Mo ¹⁹	10 Do	10 Sa	10 Di	10 Fr	10 So	10 Mi	10 Fr
11 Mo ⁰²	11 Do		11 Di	11 So	11 Fr	11 So	11 Mi	11 Do	11 Mo	11 Do	11 Sa
12 Di	12 So		12 So	12 Mo	12 Sa	12 Mo ²⁸	12 Do	12 Mi	12 Di	12 Fr	12 So
13 Mi	13 Mi		13 Di	13 So	13 So	13 Di	13 Fr	13 Do	13 Mi	13 Sa	13 Mo ⁵⁰
14 Do	14 Mo ⁰⁷	14 So	14 Mi	14 Fr	14 Mo ²⁴	14 Mi	14 Sa	14 Di	14 Do	14 So	14 Di
15 Mo	15 Mo	15 Mo ¹¹	15 Do	15 Sa	15 So	15 Do	15 So Mariä Himmelfahrt	15 Mi	15 Fr	15 So	15 So
16 Di	16 Di	16 Di	16 Fr	16 So	16 Fr	16 Fr	16 Mo ³³	16 Do	16 Sa	16 So	16 So
17 So	17 Mi	17 Mi	17 Sa	17 Mo ²⁰	17 So	17 Sa	17 Di	17 Fr	17 So	17 Mi Buß- und Betttag	17 So
18 Mo ⁰³	18 Do	18 Do	18 So	18 Di	18 So	18 So	18 Mi	18 Sa	18 Mo ⁴²	18 Do	18 Sa
19 Di	19 Fr	19 Fr	19 Mo	19 Mi	19 Sa	19 Mo ²⁹	19 So	19 So	19 Di	19 Fr	19 So
20 Mi	20 So	20 Sa	20 Do	20 Do	20 So	20 Di	20 Mo	20 Mo Weltkindertag ³⁸	20 Mi	20 So	20 Mo ⁵¹
21 Do	21 Mo	21 So	21 Fr	21 Fr	21 Mo ²⁵	21 Mi	21 Sa	21 Di	21 Do	21 Mi	21 Di
22 Fr	22 Mo ⁰⁸	22 Do	22 Do	22 Sa	22 Di	22 Do	22 So	22 Mi	22 So	22 Do	22 Mi
23 Sa	23 Di	23 Di	23 Fr	23 So	23 Mi	23 Fr	23 Mo ³⁴	23 Do	23 Sa	23 Di	23 Do
24 So	24 Mi	24 Mi	24 Sa	24 Mo	24 Do	24 Sa	24 Di	24 Mi	24 So	24 Mi	24 Fr
25 Mo ⁰⁴	25 Do	25 Do	25 So	25 So	25 Fr	25 So	25 Mo	25 Sa	25 Mo ⁴³	25 Do	25 Sa
26 Di	26 Fr	26 Fr	26 Mo	26 Mi	26 Sa	26 Mo ³⁰	26 So	26 So	26 Di	26 Fr	26 So
27 So	27 Sa	27 Sa	27 Do	27 Do	27 So	27 Di	27 Mi	27 Mo ³⁹	27 Mi	27 Sa	27 Mi
28 Mo	28 So	28 So	28 Fr	28 Fr	28 Mi	28 Mi	28 Sa	28 Di	28 Do	28 So	28 Do
29 Fr		29 Mo ¹³	29 Do	29 Sa	29 Do	29 Do	29 So	29 Mi	29 Fr	29 Mo	29 Mi
30 Sa		30 Di	30 Fr	30 So	30 Fr	30 Fr	30 Mo ³⁵	30 Do	30 Sa	30 Di	30 Do
31 So		31 Mi		31 Mo ²²	31 Sa	31 Sa	31 Di	31 So	31 So Reformationstag		31 Fr

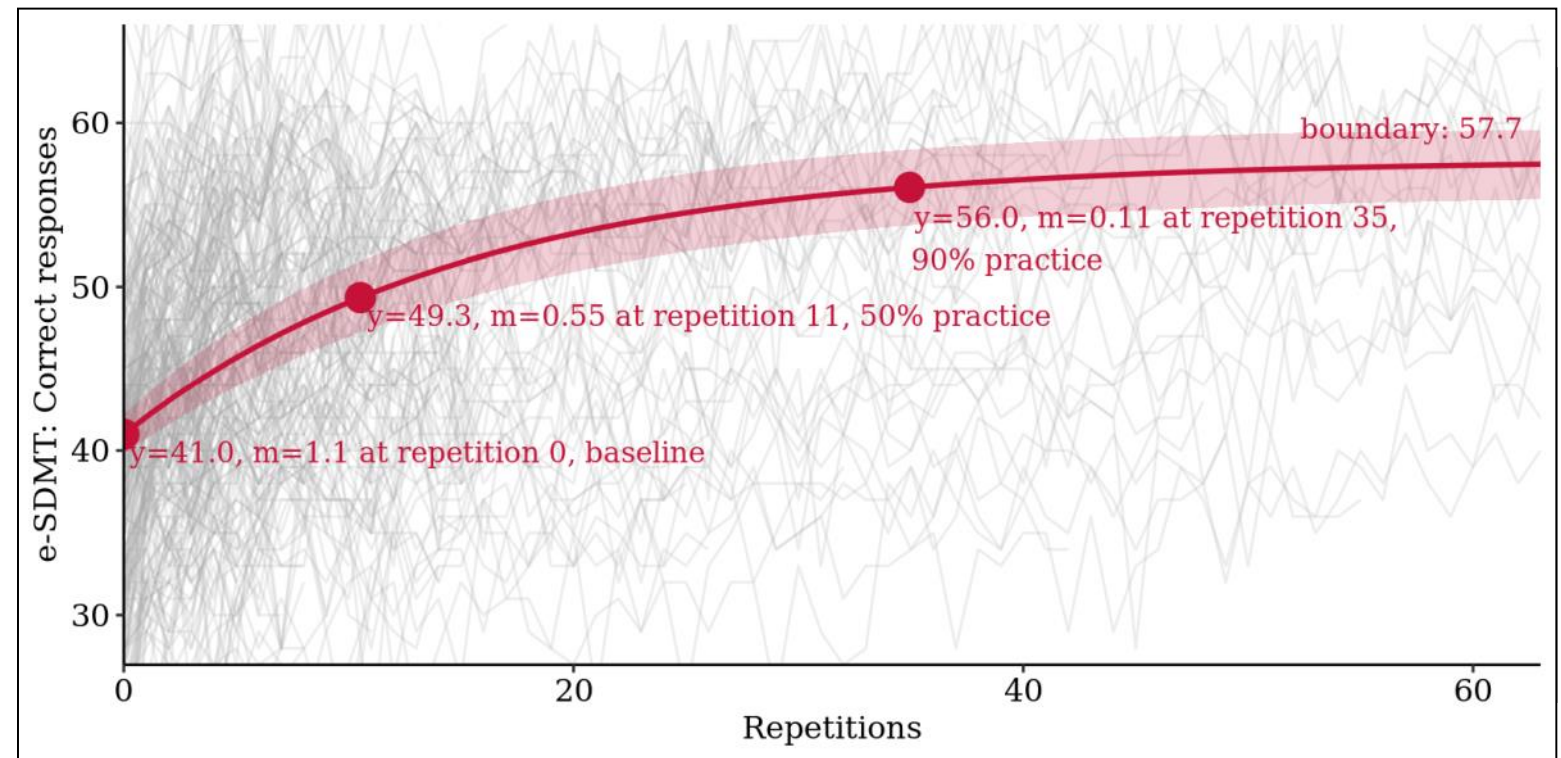
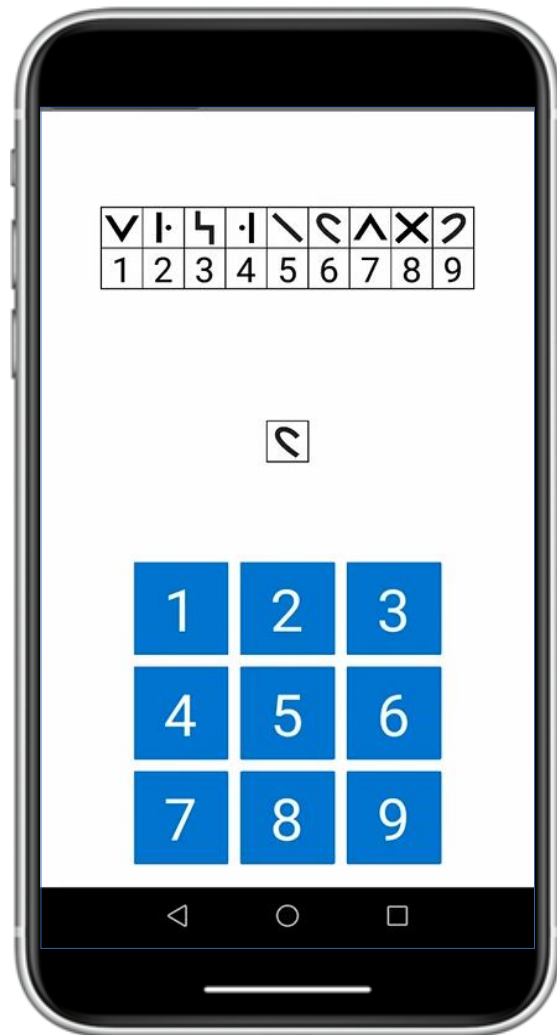
Promises of Digital Biomarkers

- **Daily, weekly or monthly tests**
 - Registration of disease course with high temporal resolution
- **Tests at home and in natural environment**
 - High ecological validity
- **Objective algorithms**
 - Less intra- & inter-rater-variability
- **Potentially better sensitivity to change**
- **Focus on topics relevant for people with MS**

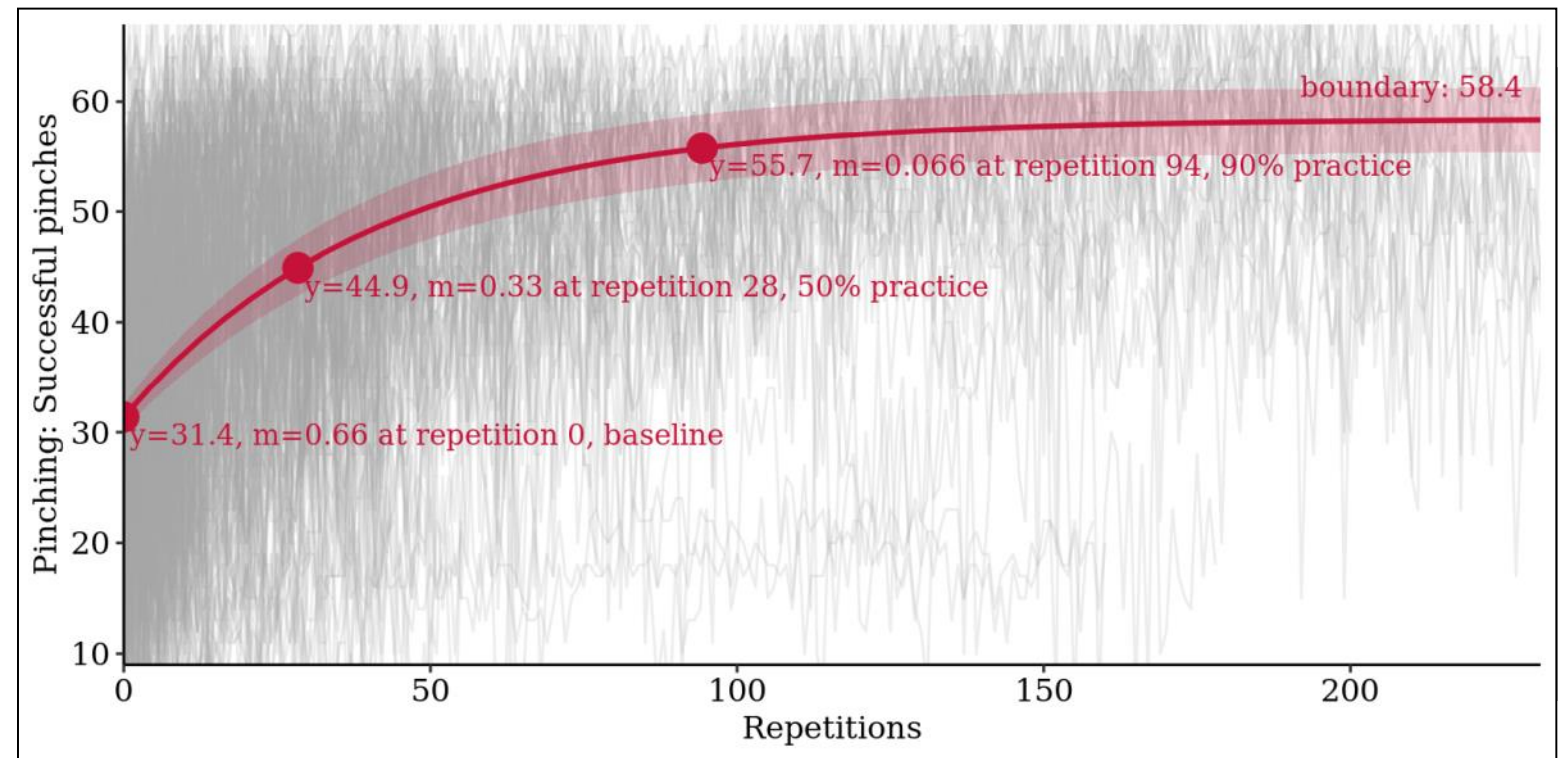
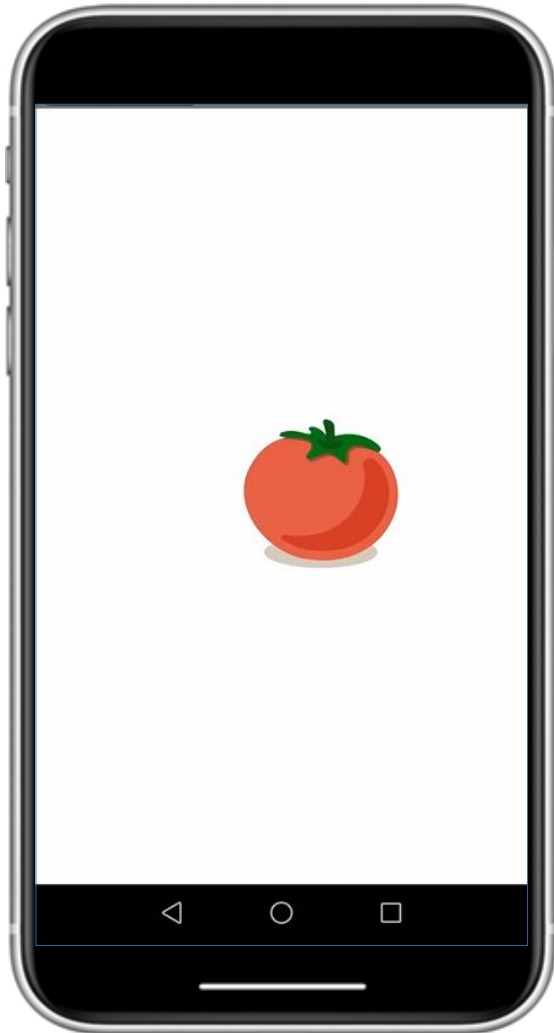
Learning & Practice Effects: Case Study

Study	Floodlight Open
Sponsor	Roche
Duration	5 weeks up to >1 year
N PwMS Selected	171-264
Proportion Female	71%
Age, median (IQR)	50 (42-58)

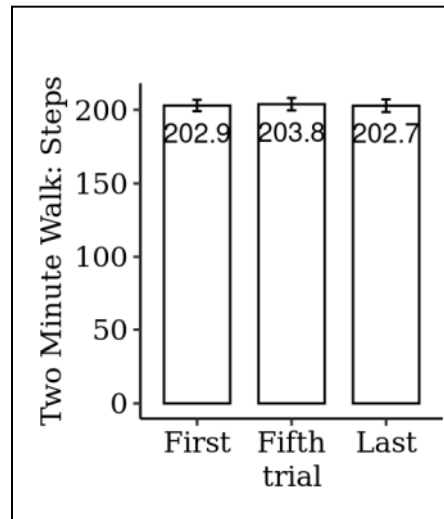
Cognition: Symbol Digit Modalities Test

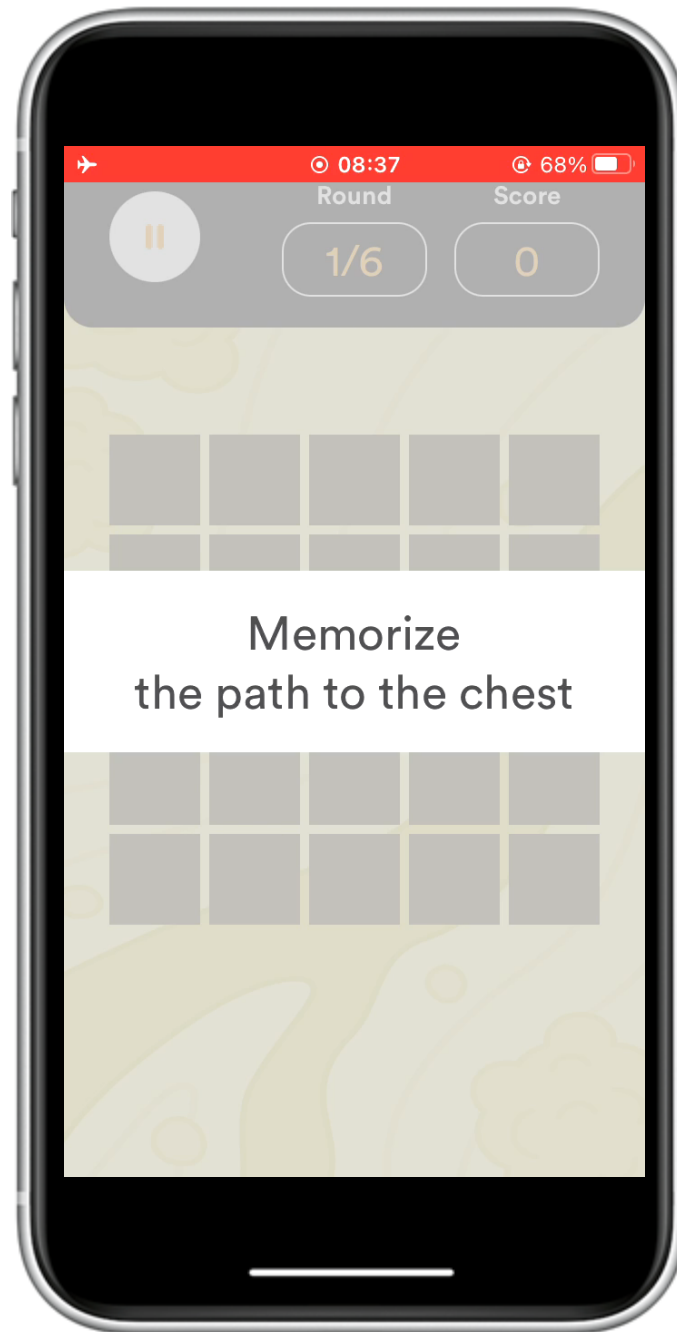


Dexterity: Tomato Pinching



Mobility: 2-Minute Walk







What do we measure with dreaMS?

Smartphone Tests (active)

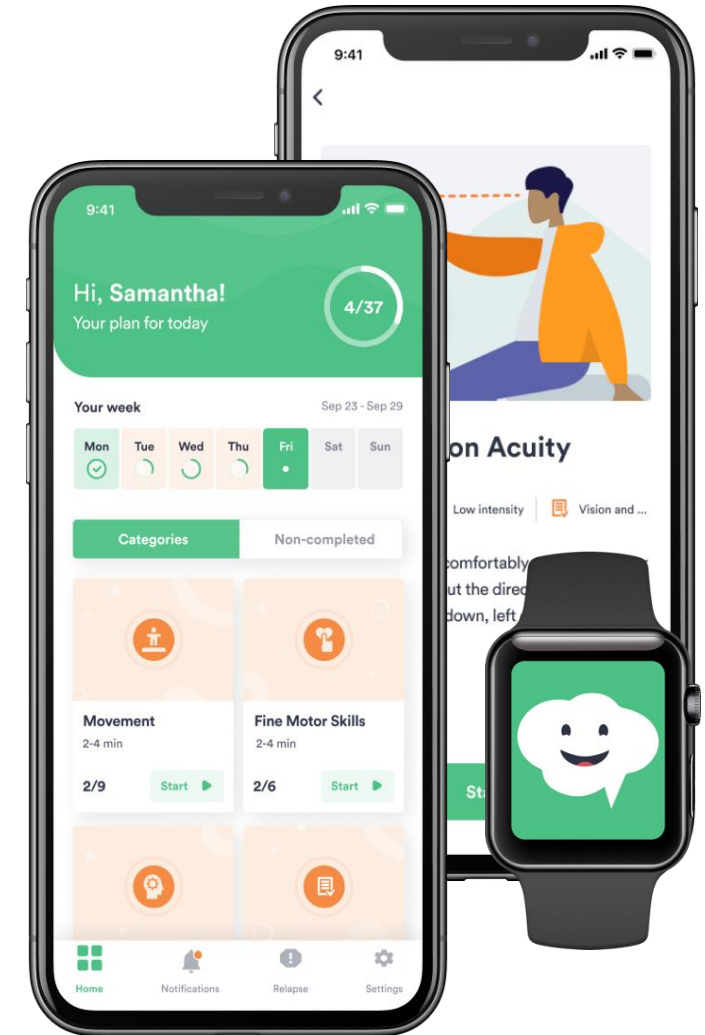
- Cognition (memory, concentration, processing, ...)
- Dexterity (screen-to-nose, catch-a-cloud, ...)
- Mobility & Balance (walking, climbing stairs, Romberg, ...)
- Vision (acuity, contrast)

Surveys (active)

- Symptom severity
- Fatigue
- Quality of Life

Smartwatch Monitoring (passive)

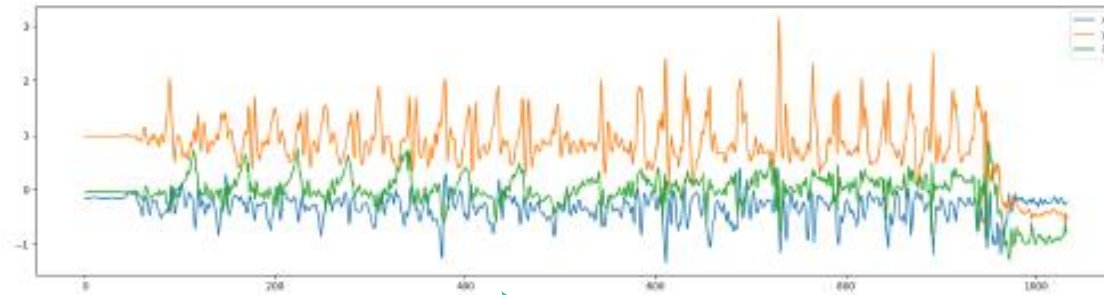
- Physical activity
- Steps
- Heart rate
- Calories
- Sleep



Movement Tests: From Sensors to Features

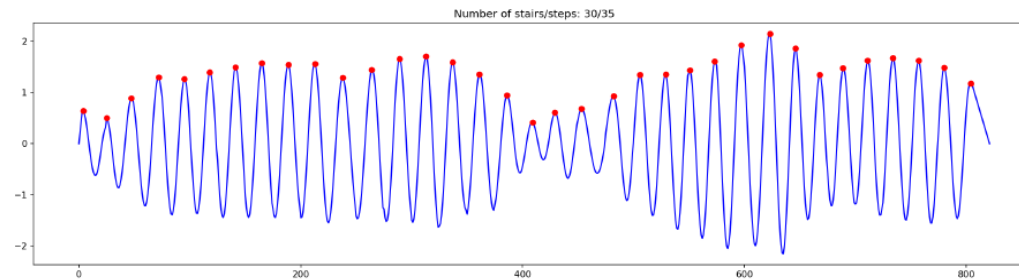


Signal detection



Raw accelerometer signal

Signal processing

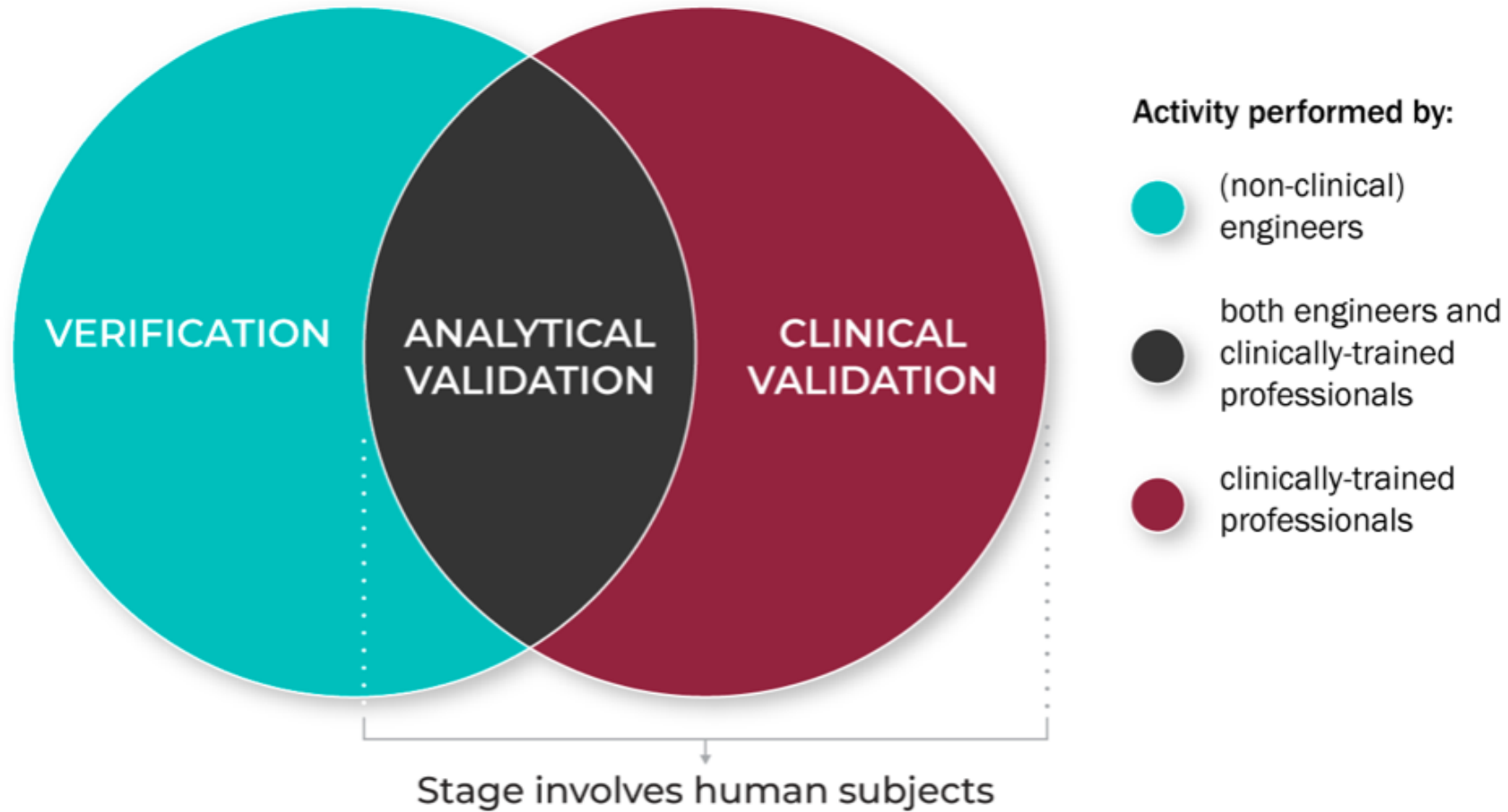


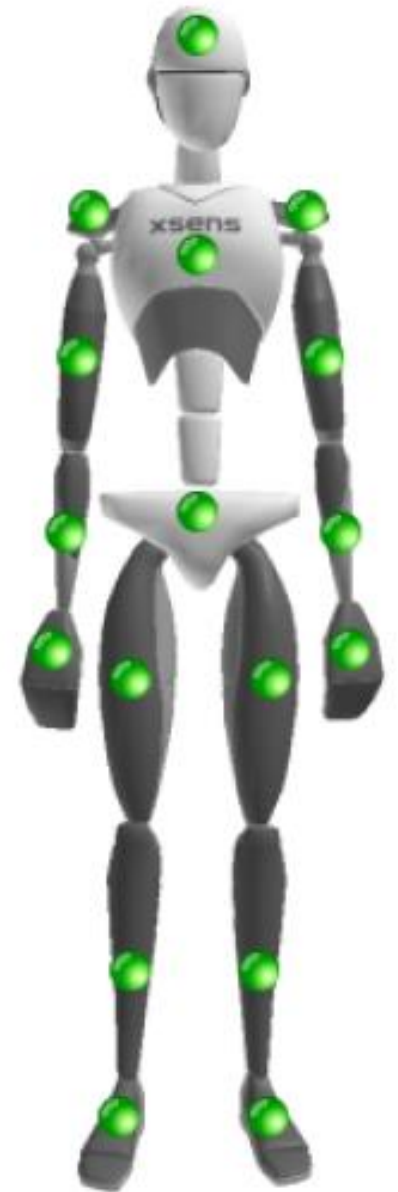
Processed signal

Feature extraction

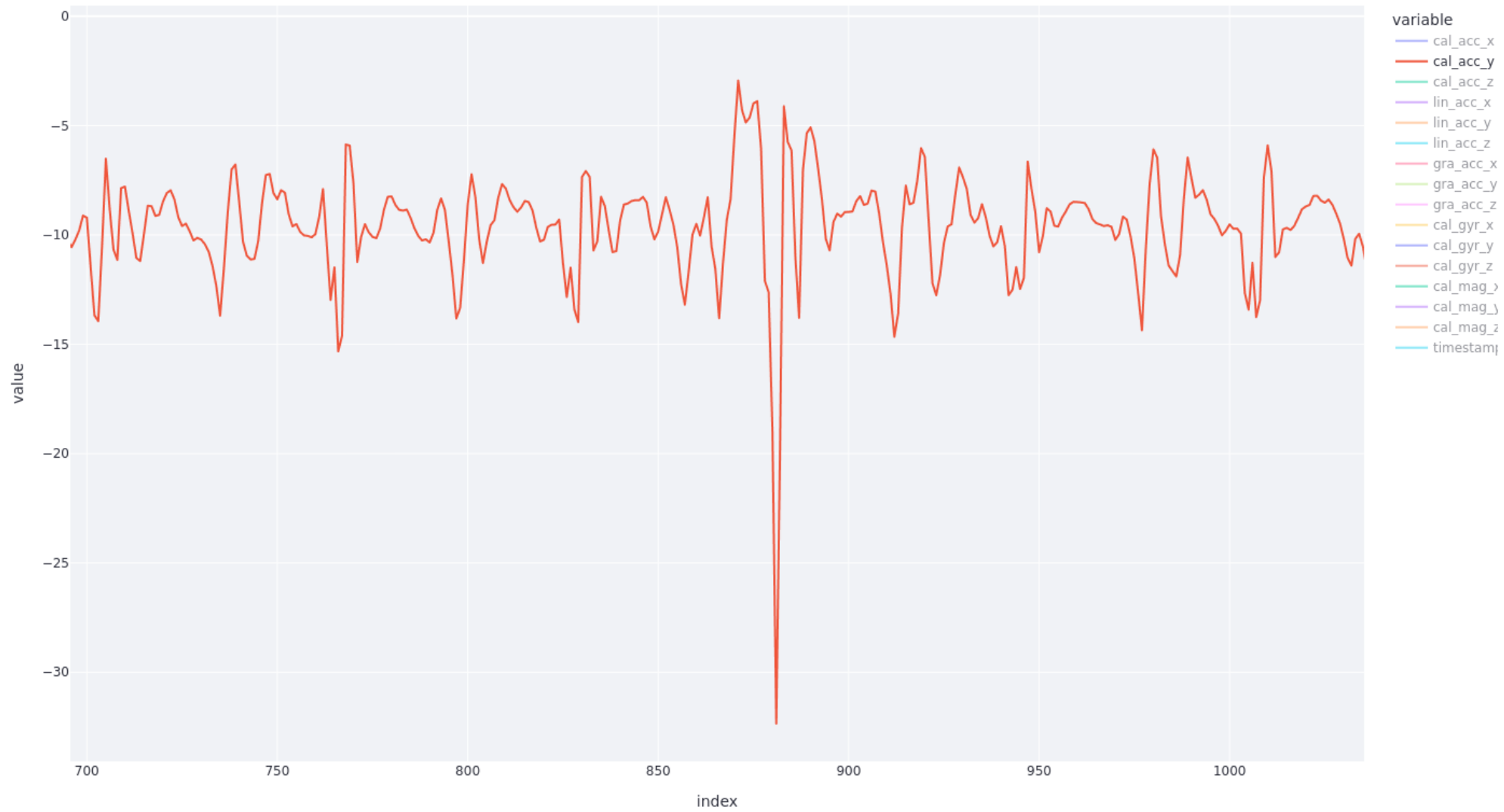
Number of steps, average time per step, gait symmetry, etc.

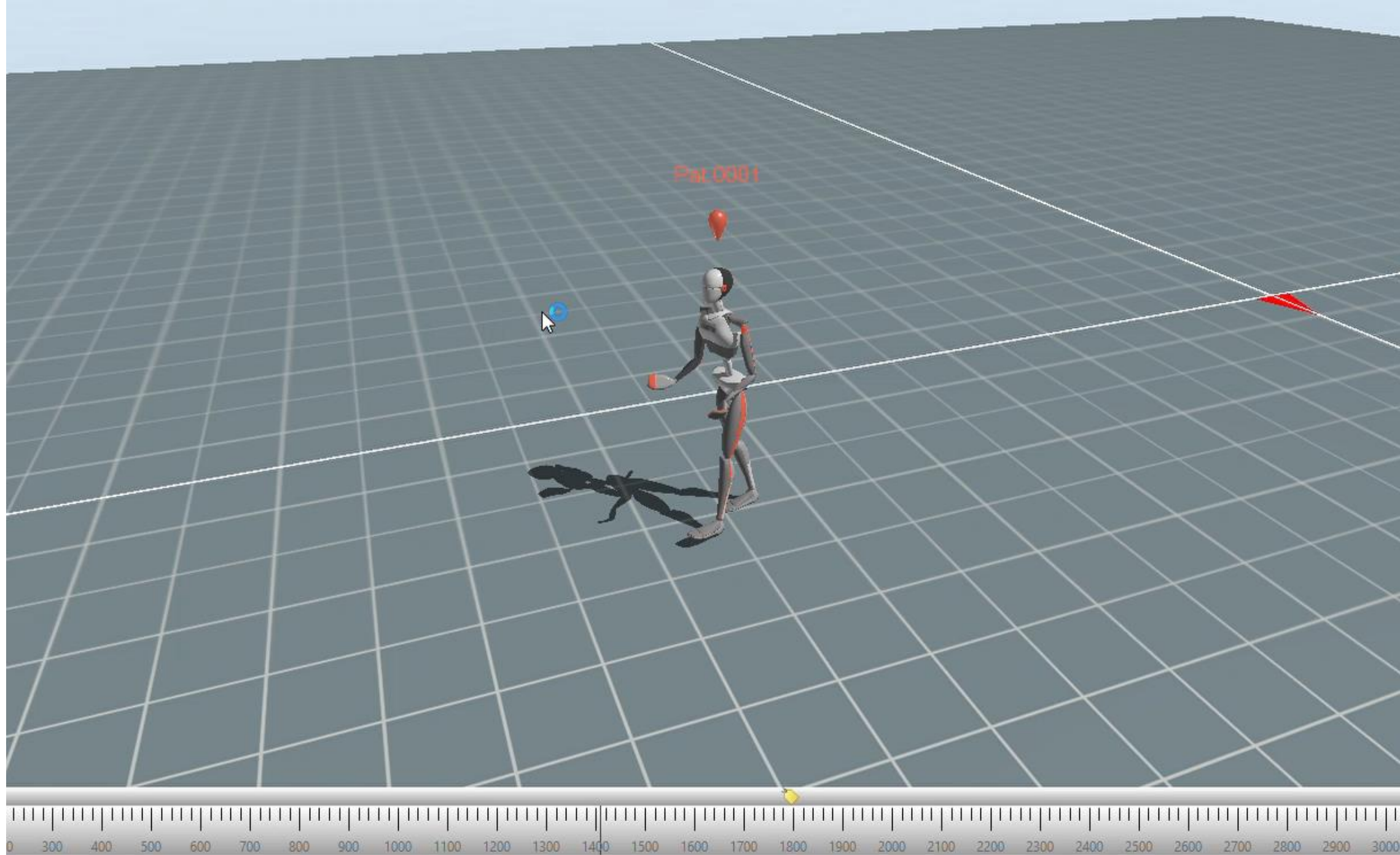
Validation: V3 Concept











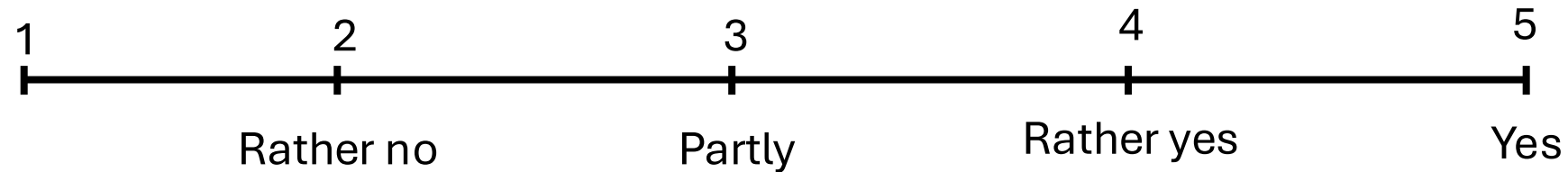
DreaMS Feasibility Study

What can we measure reliably? Which tests have acceptance? (2020-2021)

- 31 MS patients & 31 matched healthy controls, [NCT04413032](#)
- Duration: 6 weeks per participant
- Frequent active challenges, roughly 10 minutes per day, 5 days a week
- Results:
 - All 11 tests produced at least one reliable feature ($ICC \geq 0.6$ or median $CV < 0.2$)
 - All 11 tests were perceived as meaningful among PwMS according to interview and Likert scale

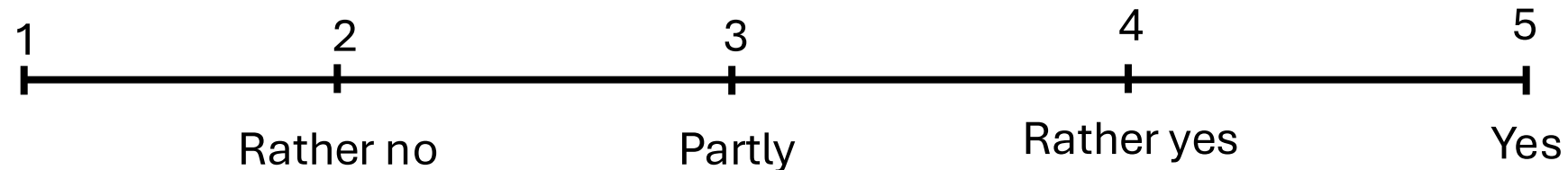
Overall impression (all 62 participants):

Did you like this exercise in principle?



MS-relevance (31 PwMS only):

Do you think this exercise makes sense for people with MS?



Test	Overall impression (n=62)	MS Meaningfulness (n=31)
Movement		
U-Turn	4.10 ± 1.10	4.45 ± 0.89
Two minute walk	4.23 ± 1.06	4.32 ± 0.98
Climbing stairs	4.15 ± 1.07	4.52 ± 0.85
Musical chairs	4.28 ± 1.00 ¹	4.53 ± 0.73 ²
Balance		
Arm balance	4.21 ± 1.02 ¹	4.67 ± 0.66 ²
Standing balance	3.97 ± 1.21 ¹	4.27 ± 1.08 ³
Dexterity		
Screen-to-nose	4.00 ± 0.99	4.42 ± 0.92
Catch-a-cloud	4.55 ± 0.80	4.35 ± 1.02
Cognition		
m-SDMT	3.89 ± 1.33	4.39 ± 1.02
Vision		
Near vision	3.74 ± 1.28	4.39 ± 0.92
Low contrast	3.84 ± 1.22	4.29 ± 0.94

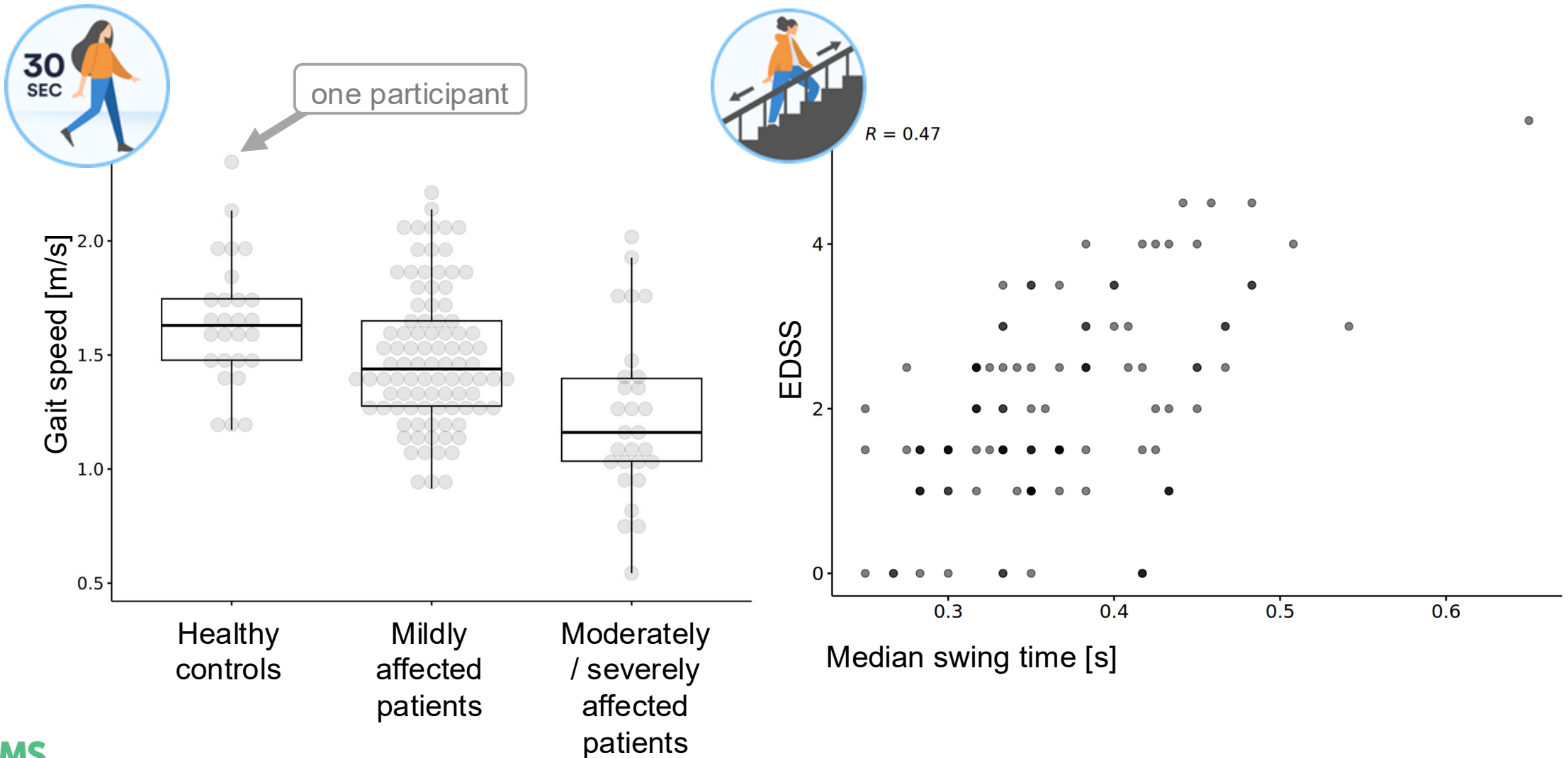
DreaMS Validation Study

Are the digital biomarkers valid & relevant? (2022-2026)

- 275 people with MS & 50 healthy controls, [NCT05009160](https://clinicaltrials.gov/ct2/show/study/NCT05009160)
- Duration: 2 years per participant
- Lower frequency of active challenges, only a few per week
- Primary outcomes:
 - Correlation of digital features with clinical reference tests (EDSS, T25FW, 9-HPT, neuropsychological testing, ...)
 - Prediction of worsening in the clinical reference test by changes in the digital biomarkers over the two-year follow-up



Preliminary Results



Summary

- Digital biomarkers can address unmet needs in the clinical monitoring of people affected by MS and other neurological diseases.
- The use of consumer wearables and smartphones improves availability and scalability of sensor-based measurements.
- Learning and practice effects seem to mostly affect active tests of cognition and dexterity, less of mobility.
- The dreaMS app reliably assesses features reflecting key functional domains meaningful to people affected by MS.
- Thorough longitudinal validation is required before outcomes based on sensor data can be used as digital endpoints.

Thank You!



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