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ORIGINAL COMMUNICATION

Feasibility of a smartphone application for remote use in spastic ataxias: an 8-week long-term PROSPAX study

Ilse H. J. Willemse[1] · Sabato Mellone[2,3] · Carlo Tacconi[3] · Filippo M. Santorelli[4] · Ivana Ricca[4] · Sara Satolli[4] · Stephan Klebe[5,6] · Nicole Jeschonneck[5,6] · Winfried Ilg[7] · Rebecca Schüle[8,9] · Matthis Synofzik[10,11] · Jorik Nonnekes[12,13] · Bart P. C. van de Warrenburg[1]

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Abstract

Background Digital biomarkers show significant potential and are emerging as outcome measures in clinical trials in spastic ataxias (SPAX). Research on the performances of digital biomarkers in home environments remains limited.

Objectives To evaluate feasibility, user adherence, time-of-day and learning effects, and consistency across settings of the SPAX-app for home monitoring in clinical trials. The app contains four tasks assessing gait, standing balance, and finger and hand movements, along with a patient-reported outcome measure (PROM).

Methods We conducted an 8-week long-term study in 38 SPAX patients and 10 healthy controls. Subjects first answered the SPAX-app PROM and performed tasks during one in-clinic session. Severity of ataxia and spasticity were assessed by clinician-reported outcome measures (ClinROs). Subjects then performed the tasks and answered the PROM twice a week in the morning and evening at home.

Results The SPAX-app showed high feasibility for finger and hand movement tasks (92%), but limited feasibility for gait (47%) and stance (63%) tasks. Among those able to perform the tasks, adherence was high (81%). A significant difference ($p < 0.01$) was found between morning and evening assessments by PROMs in SPAX. Results remained stable across the day and repeated assessments, except for the inter-onset interval in finger tapping ($p = 0.002$ and $p = 0.020$, respectively). Strong correlations were observed between tasks performed at home and in the clinic. Motor outcome measures correlated well with ClinROs, but not with PROMs.

Conclusion The SPAX-app is a feasible tool for remote assessment in SPAX, showing high feasibility for finger and hand movement tasks, but limited feasibility for gait and stance tasks at home. Time-of-day and learning effects were minimal. Longer-term studies are needed to assess clinical relevance.

Keywords Spastic ataxia · Smartphone application · Long-term study · Digital biomarkers · Remote monitoring

Introduction

Accurate and objective biomarkers are crucial for advancing therapeutic development in rare neurodegenerative diseases. Spastic ataxias (SPAX) represent a group of rare genetic diseases, defined by a progressive combination of lower limb spasticity, ataxia, dysarthria, and oculomotor abnormalities [1]. Currently, there is no effective treatment available for SPAX. Nevertheless, recent advances in disease-modifying therapies, such as genetic interventions, offer promising perspectives [1, 2]. There is a pressing need for objective, sensitive, and rater-independent biomarkers to adequately evaluate the efficacy of such treatments. Digital biomarkers have shown significant potential and are emerging as a preferred approach in future clinical trials [3, 4]. Several studies using wearable sensors in ataxias showed that these tools are particularly suitable for consistent and reproducible assessments, show strong correlations with disease severity, and are more sensitive to subtle changes in disease severity compared to conventional clinical scales [5–9]. Moreover, digital biomarkers can objectively capture patients' daily functioning and symptom variability—elements often missed by in-clinic assessments [5, 10].

Despite their promise, the use of sensor-based digital biomarkers in home environments remains limited. These systems are often expensive and can be challenging to operate,

Extended author information available on the last page of the article

posing practical barriers to their widespread implementation. Smartphones, given their popularity and embedded sensor technologies, may provide a feasible alternative [11].

Recently, we introduced the SPAX-app [12], a smartphone app for quantitative assessments of gait, stance, and upper limb functioning complemented by a single question that asks for the patients' global impression of disease severity. Our initial study focused on the development and validation of the SPAX-app and identified a set of four digital outcome measures of the SPAX-app for potential use in clinical trials. The first, step time, represents the average duration of individual steps during a walking task. The second, inter-onset interval in finger tapping, captures the timing between taps in a repetitive finger movement task. The third outcome measure, the standard deviation of the inter-onset interval, indicates variability in tapping rhythm. The fourth, duration of hand alternation, reflects motor speed and coordination during a task that requires rapid alternating hand movements. To further evaluate the feasibility of the SPAX-app for its intended use in clinical trials, longer-term studies conducted in the home environment are needed.

The current study aims to evaluate the feasibility and reliability of the SPAX-app for long-term home monitoring for SPAX in future clinical trials. Specifically, we here assess patient adherence to using the app four times a week on 2 days in the morning and evening over an 8-week period. An adherence rate of 75% or higher will be considered satisfactory based on earlier reported longitudinal studies in patients with a neurological movement disorder [13–15]. We also examine time-of-day effects on task performance by analyzing differences between morning and evening results. Additionally, we look at task performance consistency by analyzing differences between the SPAX-app tasks performed during an in-clinic training session and the SPAX-app tasks performed at home. Furthermore, we explore correlations between app-based and clinical (construct validity) or patient-reported outcomes, and we assess the added value of frequent home-based assessments. Finally, we analyze potential learning effects of the SPAX-app tasks.

Methods

This study was part of the PROSPAX study, a prospective, international, longitudinal, multicenter, natural history study in spastic ataxias (ClinicalTrials.gov, No: NCT04297891). The recently validated SPAX-app [12] was designed for patients with SPAX and is able to measure patients' capacity by remote, quantitative assessments of gait, stance, and upper limb functioning, and to obtain the patients' perception of health status by asking a question regarding overall symptom severity.

Patients were recruited from the Radboud University Medical Center in Nijmegen (the Netherlands), the IRCCS Fondazione Stella Maris in Pisa (Italy), the University Hospital of Essen (Germany) and the Knappschaft Kliniken in Recklinghausen (Germany). Inclusion criteria were genetically confirmed biallelic pathogenic variants in SACS or SPG7, clinically manifest disease, age > 10 years, and informed consent. Exclusion criteria were participation in an interventional study at baseline or a history of other neurological disorders. Healthy controls had no neurological or psychiatric disease, no family history of neurodegeneration, and normal findings on neurological examination.

Data collection

We carried out a long-term study in 38 SPAX patients and 10 healthy controls (HC) at home. Among the patients, 29 were diagnosed with spastic paraplegia type 7 (SPG7) and 9 were diagnosed with autosomal recessive spastic ataxia of Charlevoix–Saguenay (ARSACS). Subjects performed the four short motor tasks of the SPAX-app in their homes for 8 weeks after receiving one in-clinic training session. Subjects performed only those tasks they felt confident and safe to complete unsupervised at home, after consulting with the researcher. Subjects were asked to perform the task twice a week in the morning and evening, on one fixed weekday and one fixed weekend day of their choosing. The reason to include a morning and evening assessment was the clinical observation that many patients with SPAX and related disorders mention the impact of fatigue that emerges during the day on their symptoms, and we were thus able to test this subjective fluctuation with this design. During the in-clinic training session, severity of ataxia and spasticity were assessed by clinician-reported outcome measures (ClinRO), including the scale for the assessment and rating of ataxia (SARA) [16] and the spastic paraplegia rating scale (SPRS) [17], both assessed by a trained examiner.

Subjects rated their symptom severity from 0 to 10 in the app before completing the short motor tasks at home. Subjects performed the prescribed tasks of the app three times in a row during one measurement. During the gait task, subjects walked back and forth three times over a 10-m straight walking path, making a turn at each end, with the smartphone worn on L5 using a belt. Walking aids were allowed. During the stance task, subjects stood as still as possible for 30 s barefoot with feet together with the smartphone worn on L5 using a belt. For the finger movement task, subjects used their index and middle finger of their dominant hand to alternately tap between two buttons on the screen for 10 s. During the hand movement task, subjects tapped alternately the palm and back of their dominant hand on their thigh by rotating the wrist for 15 s. The smartphone was secured to the hand with an elastic band. Supplemental Fig. 1 depicts

smartphone placement and use during the gait, stance, finger movement, and hand movement tasks.

Data analysis

For this long-term study, we selected the most promising outcome measures of the SPAX-app—identified in our previously conducted validation study [12]—including step time, inter-onset interval in finger tapping, standard deviation of inter-onset interval in finger tapping, and the duration of hand alternation. Calculation of the outcome measures was carried out using MATALB version 2023B. For the step time, the raw acceleration data from the smartphone sensor was filtered with a 20 Hz low-pass Butterworth filter and analyzed using continuous wavelet transformation. Steps within a 10-m walking segment were identified using MATLAB's findpeaks function after detecting straight walking. The average step duration was then calculated [18, 19]. For the inter-onset interval and the standard deviation of the inter-onset interval, the app recorded the timing of button taps during the finger movement task. The interval was defined as the time between a tap with the index finger and a tap with the middle finger. For the duration of hand alternation, the raw gyroscope data from the smartphone sensor was integrated and filtered using a 0.08 Hz low-pass filter. Hand alternation was defined as the time required for one successive turn of the hand (pronation or supination). A detailed description of the SPAX-app and the data analysis is provided in our previously conducted validation study [12]. The other outcome measures of the SPAX-app that were tested in the validation study are presented in the supplementary material.

Patient adherence over the 8-week period was assessed by calculating the average number of complete days (morning and evening measurements) and the standard deviation for all SPAX subjects. We also calculated the average number of missed mornings and evenings, and the percentage of tasks performed correctly.

Statistical analyses

Statistical analysis was performed using MATLAB version 2023B. Normality testing revealed that data from both morning and evening tasks were not normally distributed for the SPAX and HC groups, except for the gait task in the HC group, which showed a normal distribution at both time points. To assess whether there was a time-of-day effect on task performance for the SPAX-app tasks and the patient-reported outcome measure (PROM) of the SPAX-app, we used the Wilcoxon signed-rank test to test for significant differences between morning and evening sessions in both groups, except for the gait task in the HC group, for which a paired t-test was applied. We only included morning measurements in the further analyses. To assess task consistency across different environments, we calculated Spearman's rho between in-clinic training results and one at-home morning measurement in both groups. To examine potential learning effects, linear mixed-effects (LME) models were fitted for each outcome measure of the SPAX-app using data from the first ten measurement sessions at home. The change from baseline of each outcome measure served as the dependent variable. The models included fixed effects for *time*, *group*, and their interaction (*time* × *group*), with *baseline* added as a covariate to account for individual differences in starting values. Random intercepts and random slopes for time were specified for each participant to capture within-subject variability over repeated measures. The model formula was:

$$Change_from_baseline \sim 1 + baseline + time * group + (1 + time|subject)$$

This approach enabled assessment of systematic changes over repeated sessions and potential group differences in these trajectories while accounting for inter-individual variability. To confirm the construct validity of the SPAX-app [12] in a larger long-term dataset of SPAX subjects, a Spearman correlation analysis was performed between outcome measures of the SPAX-app and the SARA, the SARA posture and gait subscore (SARAp&g), the SARA upper limb subscore (SARAul), and the SPRS and SPRS mobility subscore (SPRSmobility). The SARAul is composed of items five, six, and seven of the SARA and the SPRSmobility is composed of items one to six of the SPRS. Furthermore, we conducted a Spearman correlation analysis to determine whether the PROM of the SPAX-app correlates with the objective outcome measures of the four short motor tasks of the SPAX-app. In addition, we compared Spearman correlations calculated between the clinical outcome measures and a single home measurement with the SPAX-app with those calculated when incorporating SPAX-app data from 5 and 10 days of measurements at home to assess whether a large dataset results in stronger correlations. As the main analyses focused on a limited number of pre-specified outcome measures identified during prior validation and pilot work, no correction for multiple comparisons was applied. Bonferroni correction was applied only in the exploratory analyses reported in the supplementary material.

Results

Feasibility and adherence

Of the 38 SPAX patients included, two withdrew from the study and one SPAX patient had to be excluded from the data analyses because the recorded data files contained errors due to a malfunction of the smartphone. Table 1 provides an overview of the subject characteristics. Regarding

task feasibility, 18 (47%) patients were able to perform the gait task, 24 (63%) the stance task, and 35 (92%) the finger and hand movement tasks correctly. Patients who were unable to perform the gait and stance tasks were more severely affected, as reflected by higher SARA and SPRS scores. Among the patients who were able to perform the respective tasks, compliance with the planned measurement schedule was high. On average, SPAX subjects completed both morning and evening measurements for 13 days (81%) out of the requested 16 days during the planned 8 weeks. In addition, on 2 days (11%), morning measurements were missing and on 3 days (17%) evening measurements were missing. Furthermore, seven SPAX subjects (18%) voluntarily made up for one or more missed days after the intended period of 8 weeks.

During the performance of the stance task, six SPAX subjects (25%) recorded a corrective step or needed support from furniture or the wall. This occurred during 3 up to 31 (3–47%) trials of those subjects. SPAX subjects completed an average of 78 stance trials over the period of 8 weeks. All trials in which subjects recorded a corrective step or needed support were excluded from further analyses. There was no significant difference between the number of excluded trials in the morning and the evening. The majority of the SPAX subjects successfully completed the gait task as required, with 85% walking the 10-m path back and forth three times as required. Four of the SPAX subjects who performed the gait task (15%) walked the 10-m path only once back and forth and were therefore excluded. The other finger and hand movement tasks were performed correctly by all subjects. Eventually, gait data were analyzed for 18 SPAX subjects, stance data for 24 subjects, and hand and finger movement analysis for 35 subjects (supplemental Fig. 2). Three of the 18 SPAX subjects performed the gait task with a walking aid (17%), 2 used a walker, and 1 used one cane. After excluding recorded trials due to malfunction of the app, incorrect execution of the gait task (such as walking the 10-m path fewer times than required), and corrective moments observed during the stance task, we obtained an average of 15 valid morning measurements of the gait and stance task. For the hand and finger movement tasks, the average was 14.

Table 1 Characteristics of subjects with SPAX and healthy subjects

	SPAX $n=35$	HC $n=10$
ARSACS/SPG7	9/26	–
Age (years)	54 [27–72]	51 [19–72]
Male %	12 (34%)	5 (50%)
Disease duration (years)	22 [6–50]	–
SARA total score	13 [2–31]	0.3 [0–2]
SPRS total score	18 [6–40]	1 [0–7]

These averages are based on the 16 days subjects were asked to complete the tasks.

Time-of-day effects on task performance

A total of 33 SPAX subjects completed both the morning and evening measurements. Two SPAX subjects only completed morning measurements and were excluded from the analyses that assessed a potential difference between the SPAX-app tasks performed in the morning versus evening. Of all outcome measures of the motor tasks assessed by the SPAX-app, only the ‘mean inter-onset interval’ in the finger movement task showed a significant difference between morning and evening measurements in the SPAX group (Table 2). In the healthy subjects, there was no significant difference between morning and evening measurements (supplemental Table 2). A significant difference was observed in the PROM of the SPAX-app between morning and evening assessments ($p<0.01$) in the SPAX group. Subjects with SPAX rated the severity of their symptoms an average score of 4.9, on a scale of 0 to 10, with a standard deviation of 1.9 in the morning (median and interquartile range: 5 ± 3) compared to an average score of 5.1 with a standard deviation of 1.8 in the evening (median and interquartile range: 5 ± 2). Given that there was only one significant finding in the motor outcome measures of the SPAX-app, and because a higher percentage of evening measurements were missed compared to morning measurements, we only included morning measurements in the further analyses.

Task performance consistency

Three SPAX subjects were excluded from the analyses to assess the correlation between the in-clinic training session and a home measurement as there were no valid recordings of their in-clinic training session. A significant correlation ($p<0.01$) was found between the SPAX-app tasks performed during the in-clinic training session and those performed at home for all outcome measures in SPAX subject (Table 3). In the healthy subjects, there was only a significant correlation ($r=0.89$, $p<0.01$) for the inter-onset interval in finger tapping.

Long-term assessment of learning effects

Linear mixed-effects models were used to examine potential learning effects across repeated measurements at home (Table 4). Patients showed a significant decrease in inter-onset interval of finger tapping over time ($\beta=-0.002\pm0.001$, $p=0.020$), indicating slight improvement in tapping frequency (Fig. 1). All other outcome measures of the SPAX-app did not change significantly in patients (Table 4, Fig. 1). Healthy controls showed similar trends,

Table 2 Results of the morning and evening tasks of the four short motor of the SPAX-app in subjects with SPAX

SPAX	Morning	Evening	p-value* (Wilcoxon signed rank)
Gait (n = 17)	Median (IQR)	Median (IQR)	
Step time (s)	0.53 ± 0.06	0.53 ± 0.05	0.15
Finger movements (n=33)	Median (IQR)	Median (IQR)	
Inter-onset interval (s)	0.30 ± 0.12	0.32 ± 0.14	**0.02**
Inter-onset interval SD (s)	0.06 ± 0.06	0.06 ± 0.05	0.32
Hand movements (n=33)	Median (IQR)	Median (IQR)	
Duration of hand alternation (s)	0.76 ± 0.27	0.76 ± 0.29	0.39

A *p* value of ≤ 0.05 was considered statistically significant

SPAX = spastic ataxias, *SD* = standard deviation

Table 3 Correlation results (Spearman's rho) of the outcome measures of the SPAX-app performed during the in-clinic training session and at home in subjects with SPAX and HC

	SPAX			**HC**		
	In-clinic Median (IQR)	Home Median (IQR)	Spearman's Rho	In-clinic Mean (SD)	Home Mean (SD)	Spearman's Rho
Gait	(n = 18)			(n = 10)		
Step time (s)	**0.51 ± 0.04**	**0.52 ± 0.05**	**0.88****	0.46 ± 0.02	0.46 ± 0.03	0.55
Finger movements	In-clinic Median (IQR)	Home Median (IQR)	Spearman's Rho	In-clinic Median (IQR)	Home Median (IQR)	Spearman's Rho
	(n = 34)			(n = 10)		
Inter-onset interval (s)	**0.37 ± 0.18**	**0.33 ± 0.17**	**0.87****	**0.25 ± 0.14**	**0.23 ± 0.16**	**0.89****
Inter-onset interval SD (s)	**0.08 ± 0.08**	**0.07 ± 0.05**	**0.66****	0.05 ± 0.01	0.05 ± 0.02	0.14
Hand movements	In-clinic Median (IQR)	Home Median (IQR)	Spearman's Rho	In-clinic Median (IQR)	Home Median (IQR)	Spearman's Rho
	(n=32)			(n=10)		
Duration of hand alternation (s)	**0.86 ± 0.36**	**0.81 ± 0.36**	**0.93****	0.63 ± 0.11	0.65 ± 0.12	0.25

A *p* value of ≤ 0.05 was considered statistically significant. $^{*}p \leq 0.05$; $^{**}p \leq 0.01$

SPAX = spastic ataxias, *HC* = healthy controls, *SD* = Standard deviation

Table 4 Fixed effects estimates from linear mixed-effects models assessing potential learning effects (change from baseline) across outcome measures of the SPAX-app

	Fixed Effect	Estimate (SE)	p-value
Gait			
Step time	Time	-0.0002 (0.001)	0.661
	Group_HC	-0.009 (0.009)	0.293
	Baseline	-0.165 (0.076)	**0.031**
Finger movements			
Inter-onset interval	Time	-0.002 (0.001)	**0.020**
	Group_HC	-0.032 (0.017)	0.054
	Baseline	-0.266 (0.076)	**<0.001**
Inter-onset interval SD	Time	-0.0002 (0.001)	0.677
	Group_HC	-0.009 (0.010)	0.340
	Baseline	-0.295 (0.156)	0.060
Hand movements			
Duration of hand alternation	Time	-0.010 (0.008)	0.234
	Group_HC	-0.001 (0.069)	0.988
	Baseline	-0.094 (0.059)	0.112

A p value of ≤ 0.05 was considered statistically significant

HC = healthy controls, *SD* = standard deviation

but effects were generally smaller and not statistically significant (supplemental Fig. 3). Baseline performance significantly predicted change from baseline for inter-onset interval ($\beta = -0.266 \pm 0.076$, $p = 0.0005$) and step time ($\beta = -0.165 \pm 0.076$, $p = 0.031$), indicating that participants with higher initial values tended to show greater decreases over repeated sessions. None of the *time* × *group* interactions were significant for any outcome measure, indicating that the trajectory of change over sessions did not differ between patients and healthy controls.

Construct validity

All outcome measures of the SPAX-app showed a significant correlation with the SARA total score (Table 5), with the strongest correlation for the step time ($r = 0.77$) and the standard deviation of the inter-onset interval of finger tapping ($r = 0.76$). We also found significant correlations between the SARAp&g and step time ($r = 0.79$). For the SARAul, we found significant correlations for both the standard deviation of the inter-onset interval of finger tapping ($r = 0.52$) and the duration of hand alternation ($r = 0.61$). There was no significant correlation between the SPRS total score and any of the outcome measures of the SPAX-app. For SPRSmobility, we only found a significant correlation for the step time ($r = 0.55$) and inter-onset interval of finger tapping ($r = 0.61$). A larger dataset yielded stronger correlations between motor outcome measures of the SPAX-app and ClinRO's (supplemental Table 6), most pronounced in the variability measures. We found no significant correlation with the PROM of the SPAX-app and any of the other outcome measures of the short motor tasks of the SPAX-app.

Discussion

This study presents a long-term feasibility study of the SPAX-app at home over a period of 8 weeks. The results show that the SPAX-app is a reliable and feasible tool for remote assessment of motor functions in individuals with SPAX. Overall, feasibility and adherence were high, particularly for the finger and hand movement tasks, whereas feasibility for gait and stance assessments was more limited in the unsupervised home environment. While we found a significant difference between the PROM of the SPAX-app reported in the morning and evening in subjects with SPAX, the motor outcome measures appeared stable during the day, with the exception of the mean inter-onset interval in finger tapping. Furthermore, significant correlations were found between the tasks performed at home and in the clinic for subjects with SPAX. A learning effect was only observed

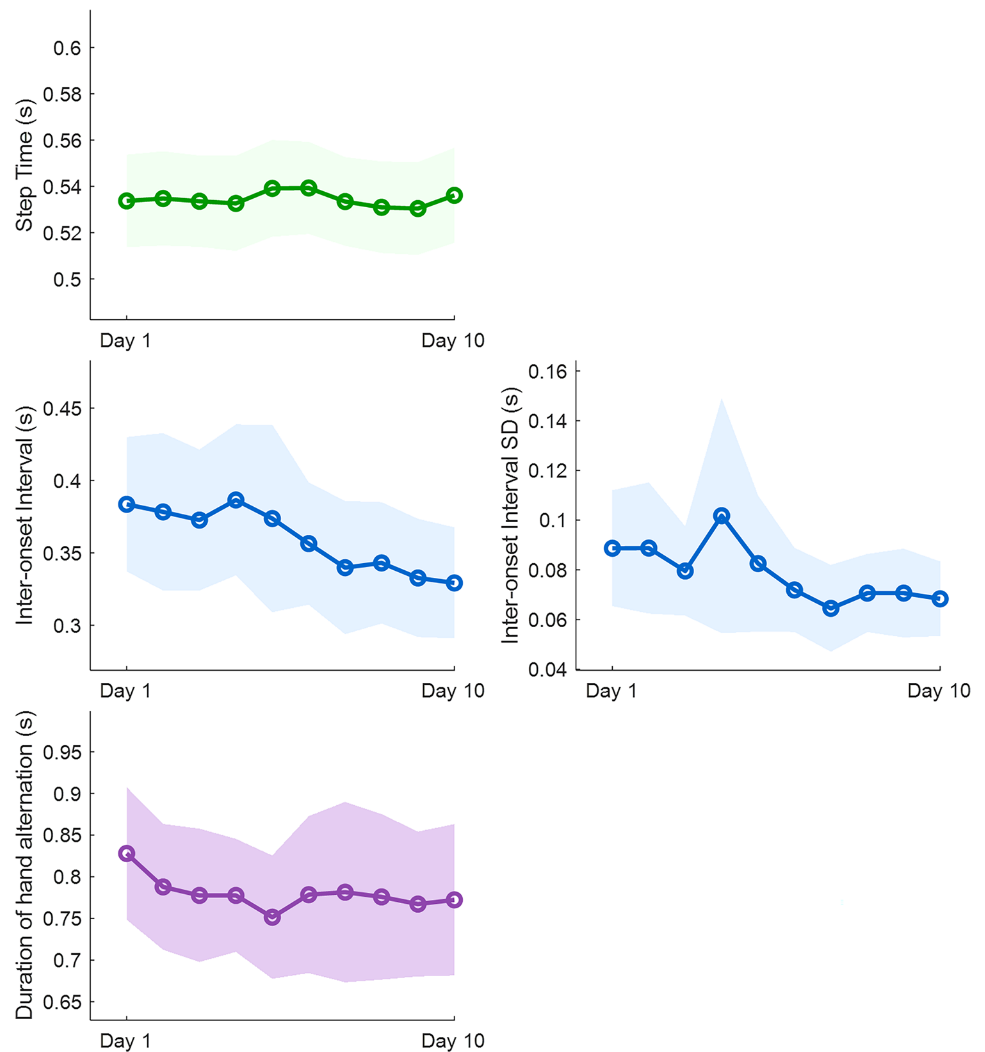

Fig. 1 Outcome measures of the SPAX subjects over time for the gait task (green), finger movement task (blue), and hand movement task (purple) of the SPAX-app

for the inter-onset interval in finger tapping for subjects with SPAX. The reported construct validity was in line with the results of the laboratory-based validation study [12]. However, no correlations were found between the PROM of the SPAX-app and any of the motor outcome measures of the app.

For the gait and stance tasks, a higher number of subjects and trials then expected had to be excluded due to incorrect task execution. This was particularly evident in the gait task, where participants failed to follow the instructed walking distance, resulting in four subjects (15%) being excluded. In the stance task, six subjects (25%) reported incorrect execution; the need for corrective steps or external support suggest that some participants may not have had the physical ability to complete the task as intended. These findings indicate that these tasks are more prone to incorrect execution when performed unsupervised at home in comparison to the finger and hand movement tasks of the SPAX-app. This is a relevant outcome of our study, as gait will be a prioritized outcome domain in future SPAX trials. In line with our earlier validation study, stance measures showed poor clinical validity (supplemental Table 5). Combined with the lack of consistency between home and clinic assessments for most stance measures (supplemental Table 3), this indicates that the current static stance task of the SPAX-app may be unsuitable for this patient group.

The presence of a time-of-day effect in only one outcome measure of the SPAX-app in subjects with SPAX was somewhat unexpected as many individuals with SPAX indicate that their symptoms increase in the evening, which was reflected in the outcome of the PROM of the SPAX-app. No previous study has investigated the time-of-day effect on PROMs in (spastic) ataxias. However, the absence of time-of-day effects on the motor outcome measures of the SPAX-app is advantageous in the context of clinical trials. It suggests that the motor outcome measurements are consistent during different times, thereby reducing variability unrelated to the intervention or disease progression. The

Table 5 Cross-sectional results (Spearman's rho) of the outcome measures of the SPAX-app with clinical measures in subjects with SPAX

	SARA total	SARAp&g	SARAul	SPRS	SPRS mobility	SPAX-app question
Gait (n=18)						
Step time	**0.77****	**0.79****	-	0.39	**0.55***	0.05
Finger movements (n=35)						
Inter-onset interval (s)	**0.55****	-	0.34	0.40	**0.61****	0.17
Inter-onset interval SD (s)	**0.76****	-	**0.52****	0.27	0.28	-0.07
Hand movements (n=35)						
Duration of hand alternation (s)	**0.60****	-	**0.61****	0.25	0.34*	0.06

A p value of ≤ 0.05 was considered statistically significant. *$p \leq 0.05$; **$p \leq 0.01$

SPAX = spastic ataxias, *SD* = standard deviation

absence of time-of-day effects is also consistent with that of the SARAhome app [20], a tablet-based tool that enables patients to perform five items of the SARA independently at home. In this study, 12 individuals with ataxia used the SARAhome app at home for 14 days, completing assessments both in the morning and evening. The time of the assessments (morning vs evening) with the app had no effect on the outcome measures.

The consistent performance of tasks across home and clinical settings in SPAX subjects strengthens the reliability and interpretability of the data and increases the sensitivity to detect true treatment effects for future clinical trials. To our knowledge, this is the first study to directly compare smartphone task performance between clinical and home settings in this population, which limits direct comparison with existing literature but offers unprecedent solutions for remote monitoring in future trials.

The results of the construct validity are in line with our laboratory-based validation study [12] for all outcome measures, except for the standard deviation of the inter-onset interval in finger tapping that showed a notable stronger correlation during the long-term study. No correlation between PROM in SPAX-app (subjective score) and short motor tasks outcome measures of the SPAX-app (objective score) were found. This aligns with some previous studies that found no significant correlation in individuals with ataxia between PROMs and physician-rated motor symptoms [21, 22], but contrasts with other that reported significant associations between PROMs and digital motor outcomes [23–25]. These mixed findings may reflect differences in the sensitivity of the PROMs used. For example, using only a single question regarding symptom severity, as in the SPAX-app, may not be sufficient to capture the complexity of patients' experiences.

A learning effect was observed over time in individuals with SPAX for the finger movement task, as indicated by a significant main effect of time, whereas no such effect was detected in healthy controls. Due to their motor impairments, SPAX patients may benefit more from repeated task exposure, allowing gradual adaptation and refinement of motor control [26]. The observed learning effect might therefore represent a combination of motor adaptation, compensatory strategy development, and task familiarity. In contrast, healthy individuals likely perform near ceiling level after the in-clinic training session, limiting the possibility of further improvement and thus masking any measurable learning effect. Longer measuring periods are needed to see when a ceiling level will be reached for the finger movement task in individuals with SPAX. A longer or more intensive training period may help individuals with SPAX reach their performance ceiling sooner. Reaching this plateau earlier could reduce learning-related variability and improve the reliability of long-term outcome measures in clinical trials.

In general, we observed that a large dataset yielded stronger correlations between outcome measures of the SPAX-app and clinical measures, with this effect being particularly pronounced in the variability measures. A

likely explanation is that variability measures, by definition, require sufficient data points to be reliably estimated. With limited data, estimates of within-subject variability may be unstable and more susceptible to noise, which can weaken correlations with clinical outcome measures. As the number of observations increases, the signal-to-noise ratio improves, allowing these variability measures to more accurately reflect underlying motor fluctuations or instability that are clinically relevant.

We recognize that our study has limitations. First, the small sample size in both the control and SPAX group, combined with heterogeneity in terms of disease symptoms and severity among SPAX participants, may have limited the statistical power of the analyses. Second, missing data may have introduced systematic bias, as patients with more severe symptoms were likely less able or confident to complete certain tasks in the home setting. Future studies should address this by comparing participants with and without missing data and applying methods to address missing data. Third, the follow-up period of eight weeks is relatively short and may not be sufficient to evaluate whether the outcome measures of the SPAX-app are sensitive enough to detect (subtle) changes in disease severity over time.

Conclusion

This long-term feasibility study demonstrates that the SPAX-app is a reliable and feasible tool for remote assessment of motor function in individuals with (spastic) ataxia. Feasibility and adherence were high for the finger and hand movement tasks, whereas feasibility for the gait and stance tasks was limited in the unsupervised home setting. The app showed minimal learning effects and consistent task performance across clinical and home environments, as well as no time-of-day variability in the majority of the reported outcome measures. While these findings are promising, it remains to be established whether the SPAX-app can sensitively detect disease progression or treatment effects. In addition, consistent and adequate performance of the gait and stance tasks was not always achieved, either because participants performed them incorrectly or were physically unable to complete them. Future work should focus on optimizing the feasibility of gait and stance assessments, addressing the observed learning effect in the finger movement task and validating the sensitivity and clinical relevance of these digital outcomes in detecting meaningful longitudinal changes.

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Data availability The datasets presented in this article are not readily available due to privacy or ethical restrictions. Requests to access the datasets should be directed to the corresponding author.

Declarations

Conflicts of interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethical approval We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. This study was approved by the medical ethical committee of Arnhem-Nijmegen (CMO-2020–6245). All participants provided written informed consent before enrollment.

Declaration of generative AI and AI-assisted technologies in the writing process During the preparation of this work the author(s) used ChatGPT to improve language and readability. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

References

1. Synofzik M, Schule R (2017) Overcoming the divide between ataxias and spastic paraplegias: shared phenotypes, genes, and pathways. Mov Disord 32(3):332–345. https://doi.org/10.1002/mds.26944
2. Kwei KT, Kuo SH (2020) An overview of the current state and the future of ataxia treatments. Neurol Clin 38(2):449–467
3. Klockgether T, Ashizawa T, Brais B, Chuang R, Durr A, Fogel B, Greenfield J, Hagen S, Jardim LB, Jiang H, Onodera O, Pedroso JL, Soong B-W, Szmulewicz D, Graessner H, Synofzik M (2022) Paving the way toward meaningful trials in Ataxias: an Ataxia Global Initiative perspective. Mov Disord 37(6):1125–1130. https://doi.org/10.1002/mds.29032
4. Ilg W, Milne S, Schmitz-Hubsch T, Alcock L, Beichert L, Bertini E et al (2023) Quantitative gait and balance outcomes for ataxia trials: consensus recommendations by the Ataxia Global Initiative Working Group on Digital-Motor Biomarkers. Cerebellum. https://doi.org/10.1007/s12311-023-01625-2
5. Beichert L, Seemann J, Kessler C, Traschütz A, Müller D, Dillmann-Jehn K, et al. Towards patient-relevant, trial-ready digital motor outcomes for SPG7: a cross-sectional prospective multi-center study (PROSPAX). medRxiv preprint. 2024.
6. Ilg W, Muller B, Faber J, van Gaalen J, Hengel H, Vogt IR, Hennes G, van de Warrenburg B, Klockgether T, Schöls L, Synofzik M (2022) Digital gait biomarkers allow to capture 1-year longitudinal change in spinocerebellar ataxia type 3. Mov Disord 37(11):2295–2301. https://doi.org/10.1002/mds.29206
7. Beichert L, Ilg W, Kessler C, Traschutz A, Reich S, Santorelli FM, et al. Digital Gait Outcomes for Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay (ARSACS): Discriminative, Convergent, and Ecological Validity in a Multicenter Study (PROSPAX). Mov Disord. 2024.
8. Thierfelder A, Seemann J, John N, Harmuth F, Giese M, Schule R, Schöls L, Timmann D, Synofzik M, Ilg W (2022) Real-life turning movements capture subtle longitudinal and preataxic changes in cerebellar ataxia. Mov Disord 37(5):1047–1058. https://doi.org/10.1002/mds.28930
9. Seemann J, Daghsen L, Cazier M, Lamy JC, Welter ML, Giese MA, et al. Digital Gait Measures Capture 1-Year Progression in Early-Stage Spinocerebellar Ataxia Type 2. Mov Disord. 2024.
10. Warmerdam EHJ, Atrsaei A et al (2020) Long-term unsupervised mobility assessment in movement disorders. Lancet Neurol. https://doi.org/10.1016/S1474-4422(19)30397-7
11. Landers M, Dorsey R, Saria S (2021) Digital endpoints: definition, benefits, and current barriers in accelerating development and adoption. Digit Biomark 5(3):216–223
12. Willemse IHJ, Mellone S, Tacconi C, Ilg W, Schule R, Synofzik M et al (2025) Smartphone application for spastic ataxias cross-sectional validation of a newly developed smartphone app for remote monitoring in spastic ataxias. Cerebellum 24(3):71
13. Lipsmeier F, Taylor KI, Kilchenmann T, Wolf D, Scotland A, Schjodt-Eriksen J, Cheng W-Y, Fernandez-Garcia I, Siebourg-Polster J, Jin L, Soto J, Verselis L, Boess F, Koller M, Grundman M, Monsch AU, Postuma RB, Ghosh A, Kremer T, Czech C, Gossens C, Lindemann M (2018) Evaluation of smartphone-based testing to generate exploratory outcome measures in a phase 1 Parkinson's disease clinical trial. Mov Disord 33(8):1287–1297. https://doi.org/10.1002/mds.27376
14. Lipsmeier F, Taylor KI, Postuma RB, Volkova-Volkmar E, Kilchenmann T, Mollenhauer B, et al. 2021.
15. Motolese F, Magliozzi A, Puttini F, Rossi M, Capone F, Karlinski K, Stark-Inbar A, Yekutieli Z, Di Lazzaro V, Marano M (2020) Parkinson's disease remote patient monitoring during the COVID-19 lockdown. Front Neurol 11:567413. https://doi.org/10.3389/fneur.2020.567413
16. Schmitz-Hübsch T, Baliko L et al (2006) Scale for the assessment and rating of ataxia. Neurology 66:11
17. R. Schüle, S. Klimpe, J. Kassubek, T. Klopstock, V. Mall, S. Otto and L. Schöls (2006) The Spastic Paraplegia Rating Scale (SPRS). Neurology
18. Khandelwal SW, N. Identification of Gait Events using Expert Knowledge and Continuous Wavelet Transform Analysis. Proceedings of the International Conference on Bio-inspired Systems and Signal Processing2014. p. 197–204.
19. Alafeef M, Fraiwan M (2018) On the diagnosis of idiopathic Parkinson's disease using continuous wavelet transform complex plot. J Ambient Intell Humaniz Comput 10(7):2805–2815. https://doi.org/10.1007/s12652-018-1014-x
20. Grobe-Einsler M, Taheri Amin A, Faber J, Schaprian T, Jacobi H, Schmitz-Hubsch T, Diallo A, du Tezenas Montcel S, Klockgether T (2021) Development of SARA(home), a new video-based tool for the assessment of ataxia at home. Mov Disord 36(5):1242–1246. https://doi.org/10.1002/mds.28478
21. Maas R, Schutter D, van de Warrenburg BPC (2021) Discordance between patient-reported outcomes and physician-rated motor symptom severity in early-to-middle-stage spinocerebellar ataxia type 3. Cerebellum 20(6):887–895
22. Ashizawa T, Figueroa KP, Perlman SL et al (2013) Clinical characteristics of patients with spinocerebellar ataxias 1, 2, 3 and 6 in the US; a prospective observational study. Orphanet J Rare Dis 8:177
23. Eklund NM, Ouillon J, Pandey V, Stephen CD, Schmahmann JD, Edgerton J et al (2023) Real-life ankle submovements and computer mouse use reflect patient-reported function in adult ataxias. Brain Commun 5(2):fcad064
24. Willemse IHJ, van Prooije T, Kapteijns KCJ, van de Warrenburg BPC (2025) Longitudinal assessment reveals stage-dependent utility of digital motor markers in SCA1. Mov Disord Clin Pract. https://doi.org/10.1002/mdc3.70124
25. Shah VV, Muzyka D, Jagodinsky A, McNames J, Casey H, El-Gohary M, Sowalsky K, Safarpour D, Carlson-Kuhta P, Schmahmann JD, Rosenthal LS, Perlman S, Horak FB, Gomez CM (2024) Digital measures of postural sway quantify balance deficits in spinocerebellar ataxia. Mov Disord 39(4):663–673. https://doi.org/10.1002/mds.29742
26. Draganova R, Konietschke F, Steiner KM, Elangovan N, Gumus M, Goricke SM, Ernst TM, Deistung A, van Eimeren T, Konczak J, Timmann D (2022) Motor training-related brain reorganization in patients with cerebellar degeneration. Hum Brain Mapp 43(5):1611–1629. https://doi.org/10.1002/hbm.25746

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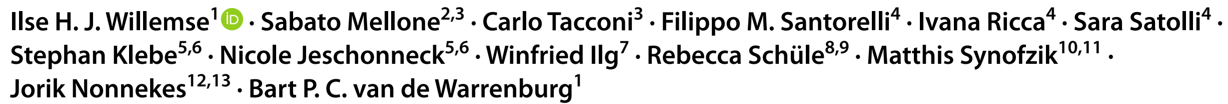
Ilse H. J. Willemse[1] · Sabato Mellone[2,3] · Carlo Tacconi[3] · Filippo M. Santorelli[4] · Ivana Ricca[4] · Sara Satolli[4] · Stephan Klebe[5,6] · Nicole Jeschonneck[5,6] · Winfried Ilg[7] · Rebecca Schüle[8,9] · Matthis Synofzik[10,11] · Jorik Nonnekes[12,13] · Bart P. C. van de Warrenburg[1]

✉ Ilse H. J. Willemse
ilse.willemse@radboudumc.nl

1 Donders Institute for Brain, Cognition and Behaviour, Department of Neurology, Center of Expertise for Parkinson and Movement Disorders, Radboud University Medical Center, PO Box 9101, 6500 HB Nijmegen, The Netherlands

2 Department of Electrical, Electronic and Information Engineering "Guglielmo Marconi", University of Bologna, Bologna, Italy

3 mHealth Technologies S.R.L., Bologna, Italy

4 Molecular Medicine, IRCCS Fondazione Stella Maris, Pisa, Italy

5 Department of Neurology, Knappschaft Kliniken Vest GmbH, Recklinghausen, Germany

6 Department of Neurology, Universitätsklinikum Essen, Essen, Germany

7 Section Computational Sensomotorics, Hertie Institute for Clinical Brain Research, Tübingen, Germany

8 Division of Neurodegenerative Diseases, Department of Neurology, Heidelberg University Hospital and Faculty of Medicine, Heidelberg, Germany

9 Center for Neurology and Hertie Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany

10 Division Translational Genomics of Neurodegenerative Diseases, Hertie-Institute for Clinical Brain Research and Center of Neurology, Tuebingen University Hospital, Hoppe-Seyler-Str. 3, 72076 Tuebingen, Germany

11 German Center for Neurodegenerative Diseases (DZNE), Otfried-Müller-Str. 23, 72076 Tübingen, Germany

12 Donders Institute for Brain, Cognition and Behaviour, Department of Rehabilitation, Center of Expertise for Parkinson and Movement Disorders, Radboud University Medical Center, Nijmegen, The Netherlands

13 Department of Rehabilitation, Sint Maartenskliniek, Nijmegen, The Netherlands