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The Institute of Neuroimmunology and Multiple Sclerosis

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Validierung des Smartphone-Akzelerometers für die Messung der Gehfähigkeit sowie der körperlichen Aktivität im Alltagskontext unter MS-Betroffenen und Gesunden

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Smartphone accelerometry: A smart and reliable measurement of real-life physical activity in multiple sclerosis and healthy individuals

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Abstract

Background: Mobility impairment is common in persons with multiple sclerosis (pwMS) and can be assessed with clinical tests and surveys that have restricted ecological validity. Commercial research-based accelerometers are considered to be more valuable as they measure real-life mobility. Smartphone accelerometry might be an easily accessible alternative.

Objective: To explore smartphone accelerometry in comparison to clinical tests, surveys and a wrist-worn ActiGraph in pwMS and controls.

Methods: 67 pwMS and 70 matched controls underwent mobility tests and surveys. Real-life data were collected with a smartphone and an ActiGraph over seven days. We explored different smartphone metrics in a technical validation course and computed afterward correlation between ActiGraph (steps per minute), smartphone accelerometry (variance of vector magnitude), clinical tests, and surveys. We also determined the ability to separate between patients and controls as well as between different disability groups.

Results: Based on the technical validation, we found the variance of the vector magnitude as a reliable estimate to discriminate wear time and no wear-time of the smartphone. Due to a further association with different activity levels, it was selected for real-life analyses. In the cross-sectional study, ActiGraph correlated moderately ($r = 0.43$, $p<0.05$) with the smartphone but less with clinical tests (rho between $|0.211|$ and $|0.337|$). Smartphone data showed stronger correlations with age (rho = -0.487) and clinical tests (rho between $|0.565|$ and $|0.605|$). ActiGraph only differed between pwMS and controls ($p < 0.001$) but not between disability groups. At the same time, the smartphone showed differences between pwMS and controls, between RRMS and PP-/SPMS and between participants with/without ambulatory impairment (all $p < 0.001$).

Conclusions: Smartphone accelerometry provides better estimates of mobility and disability than a wrist-worn standard accelerometer in a free-living context for both controls and pwMS. Given the fact that no additional device is needed, smartphone accelerometry might be a convenient outcome of real-life ambulation in healthy individuals and chronic diseases such as MS.

1 Introduction

Multiple Sclerosis (MS) is the most common autoimmune disease of the CNS and leads to an accumulation of disability by chronic inflammation and neurodegeneration (1). The patterns of disability are heterogeneous, but impaired mobility occurs in up to 75% of pwMS (2) and represents one of the most disrupting physical features of MS (3). Regarding the perceptions of bodily functions, ambulation is rated as one of the three most valuable abilities (4). Besides, walking is the most frequent type of self-selected physical activity (5) and represents with over 50% of dynamic activity over a 24-h period, the primary mode of physical activity in pwMS (6). Walking impairment could cause physical inactivity, which results in physical deconditioning, and in this negative feedback mechanism, walking impairment could be driven further down (7). In the clinical setting, walking impairment can be used to monitor disability progression, and ambulatory improvement can be used as an indicator of efficacy in therapeutic trials (8). However, while the importance of the walking ability in MS is widely accepted, the ideal measurement approach is still under discussion (9).

The Extended Disability Status Scale (EDSS), as an accepted standard of disability measurement in MS, and relies in its middle range mainly on walking abilities in the range between 20 and 500 meters (10). However, the scale suffers for its increased variability for longer walking distances and other factors like fatigue, patient´s mood and the time the test was performed. (11) EDSS also has limitations to measure small but clinically meaningful changes in ambulation and it fails to capture the performance fluctuation over time in the natural environment(12). Standard clinical performance-based measures, such as the Timed 25-foot Walk (T25FW), 2-minute walking test (2MWT), 6-minute walking test (6MWT) (13), provide objective snapshots of the day-to-day variable ambulatory capacity (14). They may not reflect the continuous walking activity in the real-world environment due to the lack of ecological validity (15). Patient-reported outcome measures (PROMS)(e.g., 12-Item Multiple Sclerosis Walking Scale (MSWS-12) (16) or Godin-Leisure-Time Exercise Questionnaire (GLTEQ) (17) are limited by recall bias and variability in self-perception of physical activity.

To that end, the total ambulatory activity undertaken in the habitual environment in performing a usual range of daily activities is recognized as the gold standard for measuring ambulatory mobility in neurological disorders (18), and there is an emerging body of research supporting the application of accelerometry for measuring physical data in MS (19,20). ActiGraph (Pensacola, FL, USA) is one

of the most common accelerometers used in research (20,21). Associations between the output of ActiGraph (i.e., activity counts, step counts, MVPA, and sedentary time) and clinical outcomes in the free-living setting have been intensively investigated (22–24). Nevertheless, there are neither standard protocols of application of commercially available accelerometers nor standard accelerometer output - for example, estimates of energy consumption, step number, or walking speed (19,25). The need and burden of wearing an additional device restricts its use to short-term usage and may, due to the perceived invasiveness, affect the ecological validity. Smartphone with built-in accelerometry might overcome this shortcoming and has been considered as a possible measurement for motion data. The cost and the burden of measurement are low due to a high usage rate in the general population and among pwMS and the lack of need for a further device (26). Studies in recent years supported the application of smartphones for assessing mobility and physical activity in clinical as well as in a free-living setting (27–30). However, there is a lack of studies investigating smartphone accelerometry as a putative outcome for neurological diseases such as MS.

Here, we aimed to investigate the value of built-in smartphone accelerometers as a valid outcome for disability and mobility compared to a wrist-worn ActiGraph in a representative group of pwMS compared to healthy controls in a free-living setting.

2 Methods

The validation and exploration of the smartphone accelerometry were done in two steps: first, we performed a technical validation course for wear time validation and selection of outcomes. Secondly, we performed a cross-sectional analysis in pwMS and healthy controls with clinical outcomes, patient-reported outcome measures (PROMS), and Actigraph measurements. The value of an outcome metric was estimated by its discriminant ability between different disability groups (e.g., mild vs. moderate impairment) and its correlation with self-reported physical activity and clinical performance-based measures.

2.1 Technical validation course

To define periods of wear time and non-wear time and to explore summary measures from the raw accelerometry data, we performed a technical validation course using 28 smartphones, Samsung Galaxy (model S4 mini) with a built-in tri-axis accelerometer. First, we collected no-wear data over 10 minutes while all smartphones were lying in different positions on a table. Then the smartphones were carried by three members from the staff for investigating wear time assessments, which

included sitting, standing, walking, running, stair climbing 10 minutes each. Passive movements were recorded in an elevator and during a bus trip.

2.2 Participants

Participants were recruited at the MS outpatient clinic at the University Medical Centre Hamburg-Eppendorf. The inclusion criteria for pwMS were (1) age 18-65 years, (2) a confirmed diagnosis of MS according to McDonald criteria 2010 (31), (3) an Extended Disability Status Scale (EDSS) (10) score below 6.5 and (4) no relapse in the last 30 days. The inclusion criteria for the controls were (1) not reporting disease with potential impact on mobility, and (2) matching the age distribution of the sample with MS. The exclusion criteria for both samples were severe medical conditions other than MS, severe cognitive impairment or any other condition that might relevantly compromise the use of a smartphone (e.g. very low visual acuity or severe ataxia). All participants gave written informed consent prior to any testing under this protocol and the local ethical review board (Ärztekammer Hamburg, PVN 5001) approved the investigation.

2.3 Procedures

After inclusion, we collected demographic data and participants filled in the questionnaires, thus Godin Leisure-Time Exercise Questionnaire (GLTEQ) (17), the Frenchay Activity Index (FAI) (32) and the International Physical Activity Questionnaire (IPAQ)(33). pwMS completed also the 12-Item Multiple Sclerosis Walking Scale (MSWS-12) (16,34). Clinic-based measures of ambulation included Five-Times Sit-To-Stand test (FTSTS), Timed 25-Foot Walk (T25FW), 2-Minute Walking Test (2MWT), 6-Minute Walking Test (6MWT) and a 3-meter Timed Tandem Walk (TTW) (13). EDSS scoring was performed within the clinical examination by a neurologist (10).

All participants were supplied with an ActiGraph (modell GT3X+) and a smartphone (Samsung Galaxy S4 mini). We asked the participants to wear the ActiGraph on the non-dominant wrist (35) and the smartphone in the habitual position like their phones for the following seven days. They were asked to wear both devices during the entire day, except for showering, swimming, or while sleeping.

2.4 Data processing

All the written data, including demography, clinical performance-based measures, and PROMS were collected in an electronic case report file. The raw Actigraph data were processed, and standard outcomes (mean vector magnitude – meanVM, daily MVPA, steps/minute) were downloaded with

ActiLife 6 software version 6.13.3 (ActiGraph, Pensacola, FL USA) in 60 seconds epoch intervals. Non-wear time was filtered out with the Choi-Algorithm (36). The smartphone accelerometer data were collected via a small Android-based application, which had been developed by the institute of neuroimmunology and multiple sclerosis (INIMS). The raw accelerometer axis (X, Y, and Z) values were filed at a sampling rate of 2 Hz.

2.4.1 Selection of smartphone outcomes

For the selection of putative smartphone outcomes in the technical validation course, we computed and explored the following summary metrics for epochs of 60 seconds (same bout length as for the actigraph): Sum of absolute axis values (sumX, sumY, sumZ) variance of axis values (varX, varY, varZ), Pearson's correlations between each pair of axes (corXY, corXZ, corYZ), sum of all absolute axis values (sumXYZ), mean absolute correlation (corXYZ), sum of absolute vector magnitude (sumVM), mean vector magnitude (VM) and mean variance of the vector magnitude (varVM). Most of the metrics reflect standard accelerometry metrics – such as the vector magnitude and sum of acceleration of selected axes(37). However, several commonly used accelerometry outcomes rely on the proper orientation in space; for example, the vertical axis counts. For smartphones, such orientation-dependent metrics are not reasonable under the concept of using the patient's device in the future. Thus, we decided to explore orientation independent metrics. We hypothesized that increasing physical activity might translate into the reduced correlation of the axes counts and increased variance of acceleration measurements.

To compare the potential metrics, the available dataset was split in a ratio of 1:1 randomly in an explorative and a validation subset. First, we used the explorative data to visually inspect boxplots of all measurements for the selection of candidates with the high discriminant ability of no-wear vs. wear time and over different activities. The potential metrics were then formally tested for discriminant abilities of wear and no wear time by ROC-analyses. Finally, we validated the metrics from the explorative dataset in the validation sample and defined cut-off values for separation of wear and no-wear time. For further analysis, all accelerometry outcomes were wear-time corrected average values.

2.4.2. Statistical analysis

For the statistical analysis, we divided the total sample into healthy controls and the pwMS. The pwMS were further divided into the following subgroups: 1. disease course (relapsing vs.

progressive) representing conceptually early and late MS, and 2. by EDSS < 3.5 vs. > = 3.5 representing a cut-off for ambulatory impairment in MS (10) (minimal ambulatory impaired vs. ambulatory impaired). We performed descriptive statistics of the demography with mean/sd, median/range or number/rates according to the nature of the data. Student´s t-test was used to detect the differences of demography, clinical performance-based metrics, PROMS, wear time, and metrics of accelerometry within the above-mentioned groups. Associations between smartphone accelerometry and ActiGraph were first estimated by spearman´s rank-order coefficient within the groups. The most correlating metric of each accelerometer was then chosen to be tested with the clinical performance-based metrics and PROMS by spearman´s rank order. We used Mann-Whitney-U-test to determine the ability of the accelerometers to separate between groups. In addition, we computed ROC-Analysis to examine the predictability of the accelerometers for disease course and severity of the disability. $P < 0.05$ was used for judging the significance level. Due to multiple comparisons, we corrected the p-values with the False Discover Rate (FDR). All analyses were performed with statistics in R.

3 Results

3.1 Technical validation and selection of outcomes

Exploration of smartphone metrics (see Figure 1 and 2 and Figure e1 and e2 in supplementary material) revealed a high sensitivity and specificity for wear time detection for sumXYZ (AUC = 0.928, $p < 0.001$, accuracy = 0.901, sensitivity = 0.874 and specificity = 0.959) and several variance metrics including varVM (AUC = 0.984, $p < 0.001$, Figure 1 A-C, accuracy =0.975, sensitivity = 0.987, specificity = 0.941). Discriminant abilities could be confirmed in the validation subset, and the AUC from the validation set did not differ from the explorative estimation for varVM ($p = 0.507$). However, varVM showed significantly higher accuracy than sumXYZ ($p < 0.001$) and was chosen for wear time detection. Moreover, both metrics tended to increase with estimated physical activity level and we used these two outcomes for further analyses (Figure 2 A and B).

3.2 Participants and clinical characteristics of the subgroups

We included 137 subjects: 70 HC and 67 pwMS. Demographic data are presented in table 1. Patients with primary or secondary progressive MS (PP-/SPMS)were elder (49.6 vs. 35.9 years) than patients with relapsing-remitting MS (RRMS). pwMS with impaired ambulation had longer disease duration (12.9 vs. 6.4) than its comparison group. Otherwise, we observed no group differences in age, BMI,

and waist. Moreover, the median EDSS in patients with primary or secondary progressive MS (PP-/SPMS) was 1.8 higher ($p < 0.001$) than in relapsing-remitting MS (RRMS).

Table 2 shows the descriptive statistics of clinical tests, patient-reported outcome measures (PROMs), and accelerometry measures of AcitGraph and smartphone. The average measurement times within seven days were 55 hours for the smartphone and 76 hours for the ActiGraph, which represent an average active wear time of 7.5 hours/day and 10.9 hours/day respectively.

3.3 Correlations between smartphone metrics and ActiGraph

First, we were interested in analyzing the correlation between standard ActiGraph outcomes, and smartphone derived metrics (see Table 3 and Supplemental Figure e3). Among all metrics, varVM correlated best with ActiGraph steps/minute within all participants (rho = 0.44, $p < 0.001$). However, this association was mainly driven by the correlation in healthy controls (rho = 0.478, $p < 0.001$), while it was clearly weaker but still significant in pwMS (rho = 0.29, $p = 0.022$).

3.4 Correlations between accelerometer outcomes, clinical performance-based measures and PROMS

Next, we investigated the association of both accelerometers with demography, clinical measures, and PROMS (Figure 4). Among the variables derived from ActiGraph, steps/minute showed within all participants the strongest, but still only weak to moderate correlations with clinical measures (2MWT, 6MWT, FTSTS,T25FW rho = |0.21| to |0.34|, $p < 0.05$) and PROMS (FAI and IPAQ, rho = |0.27|, $p < 0.05$). In healthy controls and pwMS with ambulatory impairment, MVPA had a stronger association with some of the clinical measures than steps/minute (rho = |0.28| to |0.59|, $p < 0.05$). Among all variables derived from the smartphone, varVM showed the strongest correlations among all participants. varVM correlated mildly to moderately with the demography (age and waist, rho = |0.25| to |0.49|, $p < 0.01$), the clinical measures (TTW, 2MWT, 6MWT, FTSTS, T25FW, rho = |0.56| to |0.61|, $p < 0.0001$) and with PROMS (GLTEQ and FAI, rho = |0.39| and |0.25|, $p < 0.01$).

Thus, we will describe the smartphone outcome varVM and the ActiGraph outcome steps/minute as the most correlating outcomes in the subgroups more in detail. The association of both outcomes with demography, clinical measures and PROMS are summarized in Figure 4 (for correlations of other accelerometer outcomes see supplemental material). In healthy controls varVM correlated moderately with most clinical measures (2MWT, 6MWT, F25WT and FTSTS, rho = |0.30| to |0.39|,

224 $p < 0.05$) but not with PROMs. steps/minute did not correlate with any clinical measures nor with
225 PROMs. Within all pwMSvarVM again moderately to strongly correlated with age (rho = -0.63, $p <$
226 0.0001), all clinical measures (TTW, 2MWT, 6MWT, FTSTS and T25FW, rho = |0.56| to |0.67|, $p <$
227 0.0001), GLTEQ (rho = 0.37, $p < 0.01$), EDSS (rho = -0.62, $p < 0.0001$) and MSWS-12 (rho = -0.73,
228 $p < 0.0001$). Steps/minute did not, neither within all pwMS nor in the subgroups, correlate with any
229 variable. Within minimal impaired pwMS, varVM showed moderate to strong correlation with age
230 (rho = -0.74, $p < 0.0001$), clinical measures (TTW, 2MWT, 6MWT, FTSTS and T25FW, rho = |0.45|
231 to |0.64|, $p < 0.01$), EDSS (rho = -0.602, $p < 0.0001$) and MSWS-12 (rho = -0.74, $p < 0.0001$). Within
232 ambulatory impaired subgroup, none of the accelerometer metrics correlated with any variable.
233 Overall, varVM showed in comparison to steps/mintute not only in the healthy subgroup but also in
234 pwMS a stronger association with age, clinical measures, MSWS-12 and EDSS, representing
235 walking ability and ambulatory impairment.

236 **3.5 The ability of accelerometry to differentiate between subgroups**

237 In addition, we wanted to compare the discriminant abilities of accelerometry data for MS subgroups.
238 Again, we used steps/minute and varVM as outcomes of interest. ROC-Analysis (Table 4) revealed
239 that varVM was the better classifier for differentiating pwMS from control (AUC = 0.75 vs. 0.68,
240 Figure 5). Moreover, only varVM was able to differentiate between relapsing-remitting and
241 progressive MS (AUC = 0.946, $p < 0.0001$, Figure 6) and to differentiate between severe ambulatory
242 impairment and mild ambulatory impairment patients (AUC = 0.728, $p < 0.01$, Figure 7).

243 **4 Discussion**

244 This study examined smartphone accelerometry as an outcome of real-life ambulation and physical
245 activity in healthy individuals and pwMS. To follow this aim, we analyzed the relationship of
246 putative smartphone metrics with a research-grade accelerometer (ActiGraph) during free-living
247 conditions, with objectively measured walking ability, and with self-reported physical activity.
248 Overall, results showed that the smartphone accelerometer correlated only moderately with
249 ActiGraph in HC and pwMS. However, the smartphone accelerometer seems to be more closely
250 associated with walking ability, represented by the clinical performance-based measures, such as
251 TTW, T25FW, 2- /6-MWT, FTSTS, and with ambulatory impairment, represented by MSWS and
252 EDSS. Moreover, the smartphone accelerometer differentiated the levels of ambulation among all

253 participants and ambulatory impairment among the pwMS better than the ActiGraph. In our study,
254 smartphone metrics seem more reliable than a wrist-worn research-grade accelerometer.

255 For this study, we used a new metric to capture ambulation and body motion based on accelerometry
256 data – the variance of the vector magnitude. From a conceptual point of view, the metric represents
257 the movement of the smartphone in all dimensions in a given time. The metric was chosen based on a
258 technical validation course and provided two important features: high specificity and sensitivity to
259 identify wear time periods and a positive association with increased ambulation. An advantage of this
260 metric is its independence from the orientation of the smartphone. The value of this metric was
261 evaluated in comparison to a battery of different outcomes and was chosen by applying a strict
262 selection methodology based on an explorative and a validation data set. Moreover, the promising
263 results of being a good discriminator between ambulation levels and its association with ambulatory
264 impairment metrics indicate a successful proof-of-concept.

265 The rather weak to moderate association between smartphone varVM and ActiGraph outcomes in
266 both HC and pwMS contrasts one study that android smartphones provided similar raw counts as
267 ActiGraph in a free-living setting (29). Although ActiGraph is a validated tool, most of those
268 validating studies chose the hip worn position (20,21), and the literature provides controversial data
269 for the wrist-worn position of accelerometers (12,23,38–40). However, the acceptance for the wrist-
270 worn position may be higher (39). In this study, we also used wrist-worn ActiGraph data, which
271 might explain the unexpected low to moderate correlations with clinical measures and PROMS.
272 Another reason for the lower correlation could be explained by the arm movements during the non-
273 walking time included in the high active wear time, while the participants might move the
274 smartphone mostly when they were walking.

275 Regarding the ecological validity, ActiGraph could influence the exercising behaviour and for
276 example increase the physical activity, since the notable visibility and discomfort on the wrist could
277 be perceived invasive as a "reminder". On the other hand, the possibly perceived invasiveness of a
278 wrist-worn accelerometer could be intentionally used to motivate users for more exercising.
279 Eventually, using smartphones as a ubiquitous, available measuring tool might overcome these
280 shortcomings as usual smartphone positions such as handbags, rucksacks, or pants pocket, which are
281 less perceivable and provide a high accuracy (40,41). These positions are closer to the body's center
282 of mass that has been recommended as the best sensor position(42). Thus, smartphones could refer

283 more to real life and offer higher ecological validity. However, the perceived invasiveness was not
284 studied here and needs to be addressed in future studies.

285 An important result supporting the value of our smartphone-based approach is the clear association
286 with age. Walking abilities, and especially walking speed, are known to be an important indicator of
287 health status and walking ability and age (43). Interestingly, this important coherence with age was
288 well reproducible with our smartphone metric but not with the ActiGraph. Proving a well-known and
289 fundamental relationship emphasizes the reliability of smartphone accelerometry as an outcome of
290 real-life ambulation. Furthermore, the discriminating ability of smartphone varVM confirmed the
291 assumption that smartphones could differentiate levels of walking ability and ambulatory
292 dysfunction. However, these findings are based on a cross-sectional study, and its sensitivity to
293 disability progression or improvement must be analyzed in a longitudinal setting.

294 Though, it remains uncertain which dimension of physical activity or ambulation is captured
295 explicitly by smartphones in general: There are controversial results addressing this issue in the
296 literature of former research(27,29,44). Here, our approach using a research-grade accelerometer as a
297 reference failed. However, varVM correlated much stronger with the clinical measures, representing
298 walking ability than with the PROMs, representing self-reported physical activity. Thus, we assume
299 that smartphone measures rather the walking ability than the physical activity. It might be due to a
300 measurement gap during exercising or other vigorous activities performed without the smartphone.
301 Conceptually this assumption is supported by the fact that smartphones are usually worn during
302 habitual activities like traveling, shopping, and walking outside. At the same time, it is preferably
303 placed aside during exercising and other vigorous activities. However, this assumption needs further
304 investigation.

305 The association between smartphone metrics and clinical outcomes was, in general, higher than for
306 the ActiGraph. However, both smartphone and ActiGraph correlated with clinical measures or
307 PROMs more among the ambulatory mildly to moderately impaired pwMS than those with severely
308 impaired ambulation. This links to the still open question of whether accelerometry can generally
309 measure walking ability or rather physical activity in patients with very low activity levels and
310 variable gait patterns, such as in progressive MS. However, the ability of the clinical test to mirror
311 real-life ambulation and motion is also limited, and they have a rather low ecological validity.(15,45)
312 Thus, a poor association might be due to the low performance of the real-life device or shortcomings
313 of the clinical tests. Further research is needed to provide better objective estimates of low activity

levels in more severely disabled patients. Moreover, our technical validation indicated a meaningful increase of the chosen smartphone metric with increasing physical activity. However, these findings could not be validated in the real-life setting in this study.

One of the limitations in our study was the wear time of the devices that might have been too short for reliable estimates of real-life walking or activity. The original wristlet of ActiGraph was often reported as unfeasible during specific exercising like weightlifting, on the other hand, the smartphone has a relatively short battery life and needed to be charged at least once a day. Wear time alone cannot be considered as evidence for the smartphone as an outcome of real-life activity. However, smartphone covered about 72% of the ActiGraph measurement time. Future studies need to validate against other outcomes or devices. Moreover, we asked the participants to wear the smartphone in their habitual wearing position, aiming to simulate the real-life condition and to avoid the possibly perceived invasiveness. Although the usual position like handbag, backpack, and pants pocket probably does not have differences in the accuracy of measurement(40), the smartphone secured on the upper arm showed a lower accuracy. (41) Another limitation is that it is impossible to determine if the phone estimates would remain comparable with other phone models that have not been tested. However, one of the most prominent android brands was used in this study. Finally, we only investigated a rather simple summary metric of 60s epochs, which reduces the complexity of the raw data. Advanced algorithms, for example, estimating walking speed, might improve the validity of smartphone accelerometry as it has been shown for research-grade devices. (25)

Even with these limitations, there seems are strong opportunity for smartphone accelerometry in the context of several diseases and healthy living (27,30). It might help clinicians to monitor ambulatory dysfunction, disease progress, or rehabilitation in diverse clinical conditions with high ecological validity. It could also help patients to monitor their individual changes of walking ability from a personal baseline over time and to achieve ability goals. Combined with motivational, educational tools, it may as well help to improve physical activity independent from diseases.

5 Conclusion

Smartphone accelerometry provides better estimates of mobility and disability than a wrist-worn standard accelerometer in a free-living context for both controls and pwMS. Given the fact that no additional device is needed and despite further validation, smartphone accelerometry might be a convenient outcome of real-life ambulation in healthy individuals and chronic diseases such as MS.

Moreover, activity estimates from smartphones might be more ecological valid as the perceived invasiveness of assessment is lower than for additional and clearly visible devices.

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8 Author Contributions

YZ: Design and conceptualized study; major role in the acquisition of data analyzed the data; drafted the manuscript for intellectual content.
NN: Major role in the acquisition of data; revised the manuscript for intellectual content.
JP: Interpreted the data; revised the manuscript for intellectual content.
EG: Major role in the acquisition of data; interpreted the data; revised the manuscript for intellectual content.
CH: Interpreted the data; revised the manuscript for intellectual content.
JPS: Design and conceptualized study; analyzed the data; drafted the manuscript for intellectual content.

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10 Data Availability Statement

The datasets generated and analyzed for this study are available upon request by interested researchers.

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12 Tables

Table 1 – Demographic and clinical data

	Control	pwMS	RRMS	PP-/SPMS	EDSS ≤ 3.5	EDSS > 3.5
N (Sex)	70 (47F/23M)	67 (42F/25M) (p = 0.713)	34 (18F/16M)	33 (24F/9M) (p = 0.155)	49 (32F/17M)	18 (10F/8M) (p = 0.655)
Age (years)	41.5 ± 12.8	42.9 ± 10.9 (p = 0.496)	35.9 ± 9.1	49.6 ± 7.7 (p < 0.001)	41.6 ± 11.4	46.4 ± 8.4 (p = 0.067)
Weight (kg)	71.9 ± 15.2	73.3 ± 16.8 (p = 0.613)	72.2 ± 18.5	74.4 ± 15.2 (p = 0.595)	74.4 ± 17.0	70.4 ± 16.6 (p = 0.396)
BMI	24.0 ± 3.9	24.4 ± 4.7 (p = 0.585)	24.5 ± 5.3	24.4 ± 4.2 (p = 0.905)	24.8 ± 4.7	23.3 ± 4.7 (p = 0.242)
Waist (cm)	89.1 ± 12.8	92.3 ± 14.8 (p = 0.177)	89.9 ± 16.4	94.6 ± 12.9 (p = 0.197)	93.1 ± 14.7	90.2 ± 15.5 (p = 0.499)
Disease duration (years)		8.5 ± 8.1	6.5 ± 5.6	9.7 ± 8.6 (p = 0.097)	6.4 ± 6.2	12.9 ± 9.1 (p = 0.012)
Median EDSS (range)		3 (1.0 - 6.0)	2.0 (1.0 - 5.5)	3.5 (2.0 - 6.0)	2.5 (1.0 - 3.5)	5.5 (4.0 - 6.0)

Values represent mean ± sd, if not otherwise indicated. BMI = body mass index; EDSS = expanded disability status score; p-values for group comparison (patients vs. controls, RRMS vs. PP-/SPMS, and EDSS groups) based on Chi-Square Test for rates or Student's T-Test.

Table 2 - Clinical outcomes and accelerometry data

	Control	pwMS	RRMS	PP-/SPMS	EDSS ≤ 3.5	EDSS > 3.5
Clinical test						
T25FW (sec)	4.0 ± 0.6	5.6 ± 2.8 (p < 0.001)	4.2 ± 0.8	6.8 ± 3.5 (p < 0.001)	4.7 ± 0.8	7.8 ± 3.5 (p = 0.020)
FTSTS (sec)	7.4 ± 1.7	11.7 ± 4.8 (p < 0.001)	9.6 ± 1.7	13.8 ± 5.9 (p < 0.001)	10.4 ± 2.7	15.8 ± 7.4 (p* = 0.039)
TTW (sec)	6.6 ± 1.8	11.8 ± 5.6 (p < 0.001)	8.9 ± 3.3	14.4 ± 6.2 (p < 0.001)	10.4 ± 4.1	15.8 ± 7.5 (p = 0.030)
2MWT (m)	201 ± 35	164 ± 38 (p < 0.001)	179 ± 29	148 ± 40 (p = 0.002)	176 ± 29	131 ± 41 (p = 0.003)
6MWT (m)	609 ± 75	477 ± 123 (p < 0.001)	530 ± 86	424 ± 132 (p < 0.001)	517 ± 90	362 ± 136 (p = 0.002)
PROMS						
GLTEQ	43.1 ± 27.1	25.1 ± 20.9 (p < 0.001)	30.1 ± 21.6	20.6 ± 19.2 (p = 0.105)	29.5 ± 20.9	13.9 ± 16.4 (p = 0.014)
FAI	34.6 ± 4.6	32.0 ± 6.1 (p =0.023)	32.4 ± 5.1	32.1 ± 6.8 (p < 0.868)	33.6 ± 5.1	28.6 ± 6.7 (p = 0.028)
IPAQ	7553 ± 7454	6314 ± 5919 (p =0.347)	6449 ± 5451	6188 ± 6415 (p =0.868)	6459 ± 5059	5900 ± 8099 (p = 0.805)
MSWS-12		26.4 ± 13.9	18.8 ± 9.7	34.5 ± 12.5 (p < 0.001)	21.0 ± 10.3	42.0 ± 9.4 (p < 0. 001)
Wear time of ActiGraph and smartphone						
Weartime ActiGraph minutes	4498 ± 1305	4556 ± 1692 (p =0.869)	4056 ± 1715	5038 ± 1547 (p = 0.036)	4638 ± 1437	4278 ± 2407 (p = 0.740)
Weartime smartphone minutes	3684 ± 1390	2769 ± 1980 (p < 0.005)	2783 ± 1582	2557 ± 2315 (p = 0.733)	2884 ± 2071	2081 ± 1742 (p = 0.171)
Smartphone outcomes						
meanVM	9.86 ± 0.08	9.83 ± 0.07 (p = 0.103)	9.83 ± 0.07	9.88 ± 0.07 (p = 0.007)	9.85 ± 0.07	9.87 ± 0.09 (p = 0.467)
varVM	0.485 ± 0.26	0.264 ± 0.22 (p < 0.001)	0.430 ± 0.19	0.103 ± 0.10 (p < 0.001)	0.311 ± 0.23	0.138 ± 0.16 (p = 0.007)
ActiGraph outcomes						
meanVM	2405 ± 714	2286 ± 583 (p = 0.347)	2375 ± 580	2205 ± 583 (p = 0.309)	2275 ± 592	2319 ± 575 (p = 0.805)
daily MVPA	218 ± 80	216 ± 83 (p = 0.869)	189 ± 77	240 ± 81 (p = 0.023)	213 ± 82	223 ± 88 (p = 0.791)
steps/ minute	13.5 ± 3.43	11.6 ± 2.80 (p < 0.001)	12.1 ± 2.24	11.0 ± 3.17 (p = 0.165)	11.8 ± 2.94	10.9 ± 2.24 (p = 0.421)

Values represent mean ± sd if not otherwise indicated. T25FW = timed 25-foot walk; FTSTS = five-times sit-to-stand test; TTW = 3-meter timed tandem walk; 2MWT = the two-minute walk time; 6MWT = six-minute walk time; GLTEQ = Godin-Leisure time exercise questionnaire; FAI = Frenchay Activity Index; IPAQ = international physical activity questionnaire; MSWS-12 = 12-item-MS-Walking-Scale; meanVM = mean vector magnitude; varVM = variance of vector magnitude; daily MVPA = daily moderate to vigorous physical activity. p-values for group comparison (patients vs, controls, RRMS vs PP-/SPMS and EDSS groups) based on Chi-Square Test for rates or Student's T-Test. P-values are corrected p-values through Benjamini-Hochberg

Table 3 - Spearman rho rank correlations between ActiGraph and smartphone data

		Control	pwMS
Smartphone vs. ActiGraph			
smartphone(varVM)	ActiGraph(steps/minute)	0.478****	0.288*
	ActiGraph(meanVM)	0.378**	0.201
	ActiGraph(daily MVPA)	0.169	-0.128
smartphone(meanVM)	ActiGraph(steps/minute)	0.003	0.058
	ActiGraph(meanVM)	-0.077	0.173
	ActiGraph(daily MVPA)	-0.162	0.327**
Within accelerometer itself			
smartphone(varVM)	smartphone(meanVM)	0.102	-0.243
ActiGraph(steps/minute)	ActiGraph(meanVM)	0.828****	0.796****
ActiGraph(steps/minute)	ActiGraph(daily MVPA)	0.533****	0.325*
ActiGraph(meanVM)	ActiGraph(daily MVPA)	0.727****	0.443**

FDR corrected p-values: * p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001, **** p-value < 0.0001

Table 4 - Sensitivity and specificity of accelerometry metrics to differentiate subgroups

Groups	Accelerometry	AUC	Sensitivity	Specificity	NPV	PPV	Delong´s test p-value
Control vs. patient	ActiGraph steps/minute	0.683	0.746	0.586	0.618	0.719	p = 0.286
	Smartphone varVM	0.750	0.567	0.843	0.776	0.670	
RRMS vs. PP-SP/MS	ActiGraph steps/minute	0.613	0,767	0.484	0.696	0.575	p < 0.001
	Smartphone varVM	0.946	0.939	0.853	0.935	0.861	
Impaired vs. Minimal impaired	ActiGraph steps/minute	0.567	0.426	0.750	0.308	0.833	p = 0.153
	Smartphone varVM	0.728	0.694	0.833	0.500	0.919	

ROC analyses. AUC = Area under the curve, NPV = negative predictive value, PPV = positive predictive value

The area under the curve (AUC) results were compared with Delong´s test.

Figure Legends

Figure 1 - Technical validation of smartphone metrics: Wear time detection

Exploration of different smartphone metrics revealed good discriminant abilities for sumXYZ and varVM (A and B) that could be confirmed in ROC analyses of the explorative (C) and the validation subset (D).

Figure 2 – Smartphone metrics and physical activities

Boxplots of the smartphone metrics sumXYZ (A) and varVM (B) during different activities. Both metrics also tended to increase with the activity intensity.

Figure 3 - Study flow chart

HC = healthy controls, pwMS = patients with MS, RR = relapsing-remitting MS, PP-/SPMS = primary and secondary progressive MS, EDSS = expanded disability status scale (EDSS > 3 indicates walking impairment)

Figure 4 - Association of clinical outcomes and questionnaires with smartphone varVM and ActiGraph steps/minute.

Correlogram of Spearman rho; corrected p-values for multiple comparisons through FDR; * p-value < .05, ** p-value <.01, *** p-value <.001, **** p-value <.0001

Figure 5 - Group differences between healthy control and pwMS

Left: Boxplots showing smartphone and ActiGraph metrics for controls and pwMS, * p-value < .05, ** p-value <.01, *** p-value <.001 , **** p-value < .0001. Right: ROC curves of smartphone (red) and ActiGraph (blue) showing the ability of differentiation between the groups.

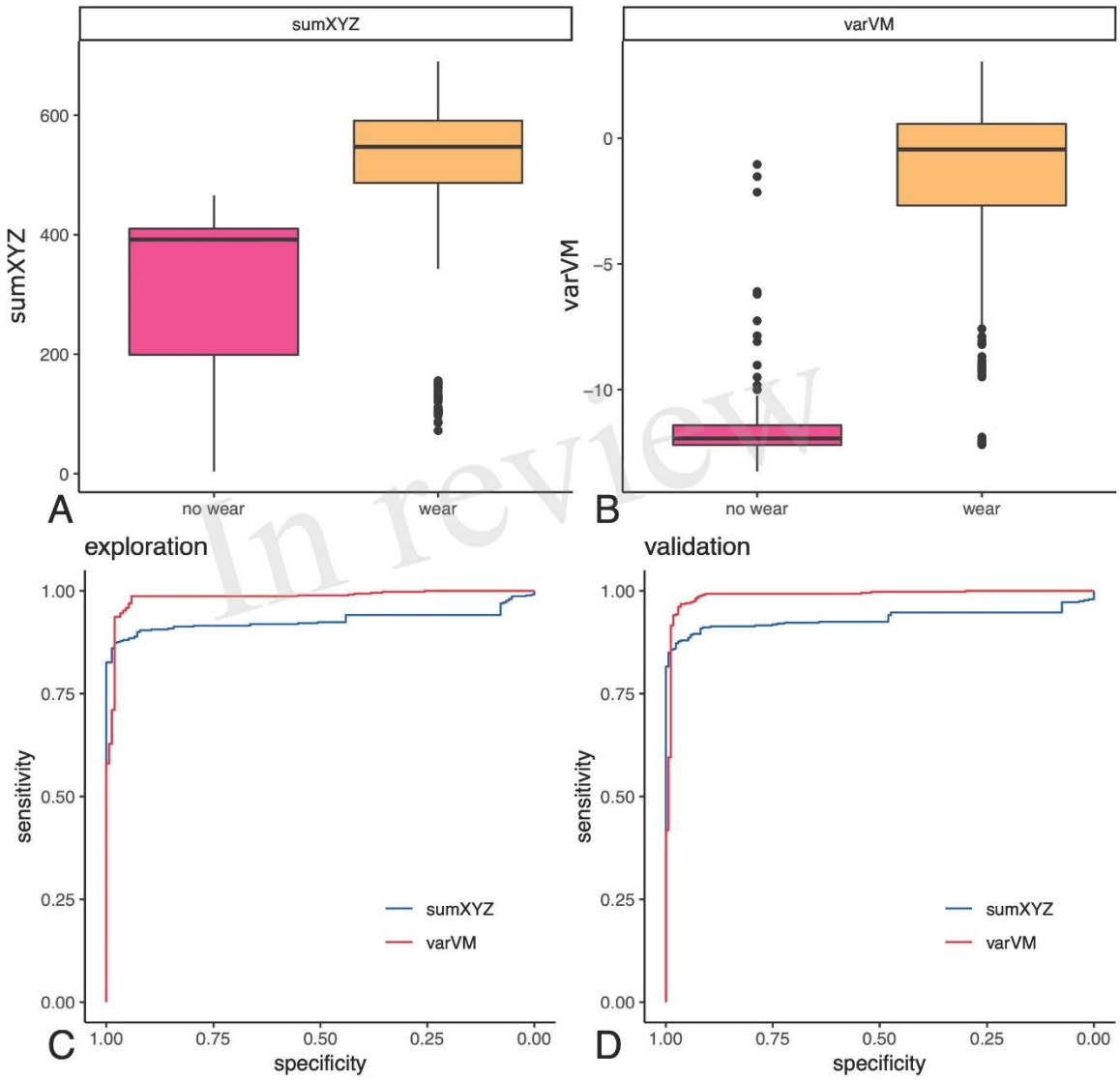
Figure 6 – Group differences between relapsing remitting and progressive MS

Left: Boxplots showing smartphone and ActiGraph metricsfor controls, progressive (or late) MS and relapsing (or early) MS. * p-value < .05, ** p-value <.01, *** p-value <.001 , **** p-value < .0001. Right: ROC curves of smartphone (red) and ActiGraph (blue) showing the ability of differentiation between the MS groups.

Figure 7 – Group differences between ambulatory minimally impaired and ambulatory impaired pwMS

Left: Boxplots showing differences between controls minimally ambulatory impaired pwMS (EDSS < 3.5) and severely impaired pwMS (EDSS > 3.5), * p-value < .05, ** p-value <.01, *** p-value <.001 , **** p-value < .0001. Right: ROC curves of smartphone (red) and ActiGraph (blue) showing the ability of differentiation of levels of ambulatory impairment.

Figure 1.TIFF



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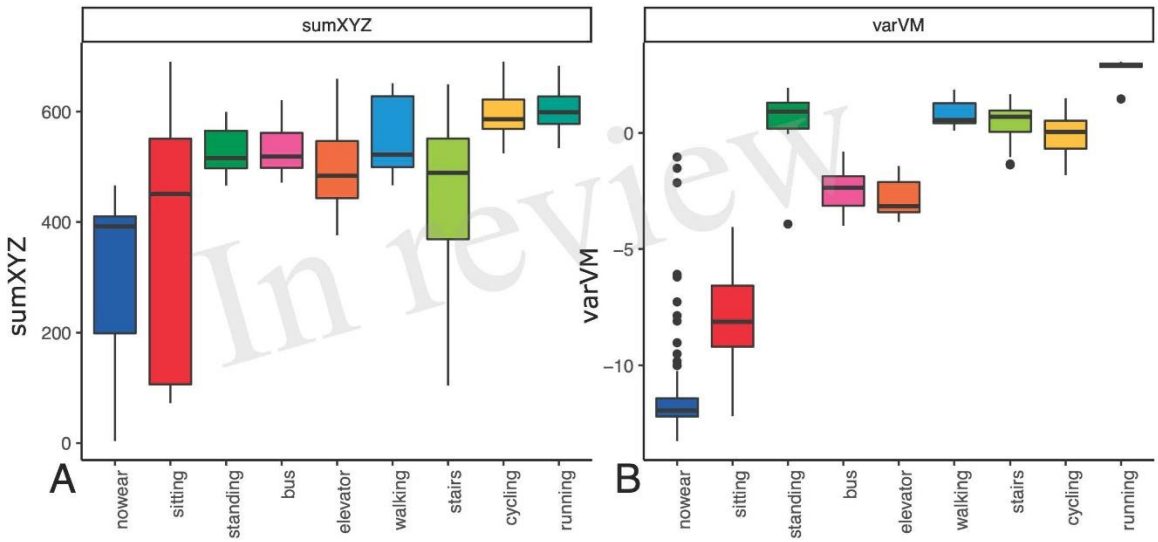

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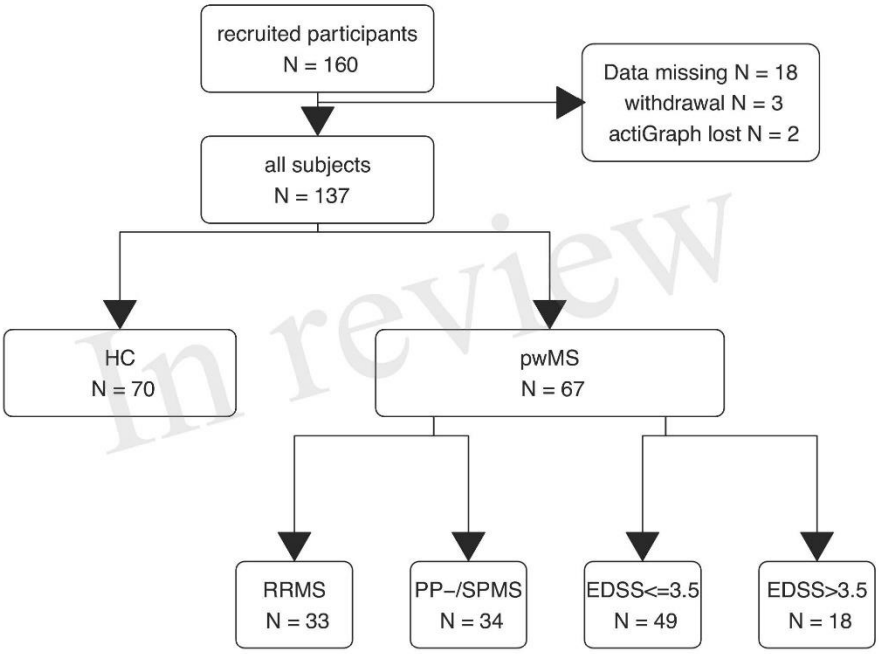

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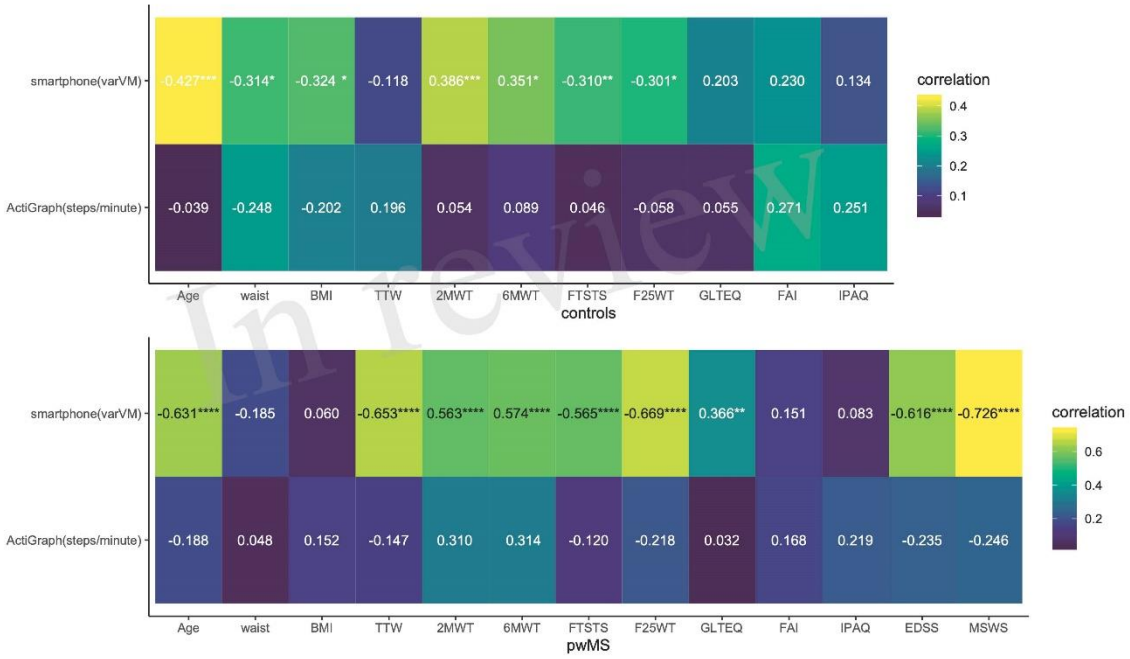

II. Darstellung der Publikation mit Literaturverzeichnis

Einleitung

Multiple Sklerose ist eine der häufigsten neurodegenerativen Erkrankungen im erwachsenen Alter. Bei über dreiviertel aller Betroffenen mit multipler Sklerose (MS-Betroffene) entwickelt sich im Krankheitsverlauf eine Beeinträchtigung der Gehfähigkeit, die sich als eines der häufigsten Symptome der multiplen Sklerose darstellt.[1] Aus der Sicht der Betroffenen wird die Gehfähigkeit als die wertvollste Körperfunktion geschätzt.[2,3] Um körperlich aktiv zu bleiben, bevorzugen die MS-Betroffenen das Gehen bzw. das „Walken".[4] In Hinsicht auf die neurologische Rehabilitation spielt die Beziehung zwischen der Gehfähigkeit, dem körperlichen Aktivitätsniveau und dem Allgemeinzustand eine große Rolle. Durch die Gehbeeinträchtigung nimmt das körperliche Aktivitätsniveau ab. Dadurch kommt es zu einer Verschlechterung des Allgemeinzustandes, wodurch weitere Beeinträchtigungen der Gehfähigkeit folgen.[5–7] In der Klinik wird die Beeinträchtigung der Gehfähigkeit als ein wichtiger Verlaufsparameter eingesetzt, um den Progress der Erkrankung zu beurteilen. Umgekehrt kann die verbesserte Gehfähigkeit beispielsweise auch als ein Indikator für die Wirksamkeit eines Medikaments dienen.[8]

Der EDSS-Score (Extended Disability Status Scale) wird standardmäßig zur Bestimmung der Schwergrade der MS-Symptome eingesetzt. Er berücksichtigt mehrere Funktionssysteme und beurteilt neben der Gehfähigkeit auch andere neurologische Defizite. Demnach können die MS-Betroffenen mit gleichem EDSS-Score unterschiedliche Gehfähigkeiten besitzen[9]. Klassischerweise werden zur Bestimmung der Gehfähigkeit verschiedene Gehtests wie Timed 25-Foot Walk (T25FW), 2-minute Walking Test (2MWT), 6-minute Walking-Test (6MWT) [10] oder Timed Tandem Walk (TTW) [11] in der Klinik durchgeführt. Ein großer Nachteil der aufgeführten Tests besteht darin, dass die Gehfähigkeit zu einem fixen Zeitpunkt erfasst wird, wobei die Leistung der Betroffenen durchaus tagesformabhängig fluktuieren kann[12]. Zudem entsprechen die Gehtests, die unter der klinischen Bedingung durchgeführt werden, nicht unbedingt der realen Gehfähigkeit unter den für die Betroffenen gewöhnlichen Umständen. Mit anderen Worten haben die Gehtests eine eingeschränkte ökologische Validität.[13]

Zur gängigen Bestimmung der Gehfähigkeit und körperlichen Aktivität gehören auch subjektive Befragungen in Form von Fragebögen, wie 12-Item MS-Walking Scale(MSWS-12), Godin-Leisure-Time Exercise Questionnaire(GLTEQ), Frenchay Activity Index(FAI) oder Short-form International Physical Acitivity Questionnaire(IPAQ)). Diese können jedoch vom individuellen Erinnerungsvermögen sowie von der variablen Selbstwahrnehmung beeinflusst werden.

Folglich sollte die ideale Bestimmung der Gehfähigkeit und des körperlichen Aktivitätsniveaus kontinuierlich, ganztäglich, in gewohnter Umgebung sowie mit einer gewöhnlichen Intensität stattfinden.[14] Seit einigen Jahren wurde die Anwendung des Beschleunigungssensors (Akzelerometers) vor dem genannten Hintergrund untersucht.[4,9,23,15–22] Allerdings existiert bisher kein Konsens für einen Standard bezüglich des Geräts, der Trageposition sowie der Parameter. [24]
Die mittlerweile sehr verbreitete Benutzung des Smartphones mit integriertem Akzelerometer bietet eine geeignete Möglichkeit für die kontinuierliche Aufzeichnung der Bewegungsdaten[25,26]. In den letzten Jahren veröffentlichten Studien zeigten bereits die ersten Indizien für die Validität bei der Anwendung von Smartphone-Akzelerometer auf.[27–30]
Ziel der vorliegenden klinischen Querschnittsstudie, ist es, das Smartphone als eine Messmethode für MS-Betroffenen zu validieren, die mit einer hohen ökologischen Validität die Gehfähigkeit sowie die körperliche Aktivität im Alltag bestimmt.

Methode

Die Validierung erfolgte in zwei Schritten: Zunächst wurde unter Laborbedingung einen technischen Validierungskurs durchgeführt, um die valide Tragezeit sowie geeignete Parameter des Smartphones zu identifizieren. Hierbei wurden mit 28 Smartphones verschiedene Aktionen für die dokumentierte Uhrzeit jeweils 10 Minuten lang durchgeführt. Zu den Aktionen gehörte beispielsweise die Flachlage auf einer ebenen Fläche, um die Liegezeit des Smartphones zu simulieren. Zwei Teammitglieder führten jeweils 14 Smartphones an verschiedenen Trageorten, wie zum Beispiel im Rucksack oder Hosentasche mit sich, und führten Bewegungen wie Gehen, Laufen, Treppensteigen durch.
Im zweiten Teil erfolgte die Querschnittsstudie mit Probanden im Alltag.
Es wurden 80 gesunde Probanden sowie 80 MS-Betroffenen rekrutiert, die den folgenden Aufnahmekriterien entsprachen. Alle Probanden sollten zwischen 18 und 65 Jahre alt sein und ein Smartphone bedienen können. Die Betroffenen sollten eine diagnostizierte multiple Sklerose (EDSS < 6,5) und während der Studie keinen akuten Schub haben.
Alle Probanden durchliefen die klinischen Tests FTSTST, T25FW, TTW, 2MWT und 6MWT. Danach füllten die Probanden die Fragebögen GLTEQ, FAI und IPAQ aus. Außerdem beantworteten die MS-Betroffenen den Fragebogen MSWS-12.
Ein ActiGraph als Armband und ein Smartphone wurden für 7 Tage geführt. Beide Geräte wurden kontinuierlich getragen, außer während des Schlafens, des Duschens und des Schwimmens.

Die Rohzählungen vom ActiGraph wurden mit der Software „ActiLife“ prozessiert. Dabei wurden mittels „ActiLife“ die Standard-Parameter wie der durchschnittliche Vektorenbetrag (mean vector magnitude), tägliche Dauer der moderaten bis schweren körperlichen Aktivität (daily MVPA) und Schritte pro Minute (steps per minute) berechnet.
Die Rohzählungen vom Smartphone wurden zuerst im Gerät selbst abgespeichert und die Daten wurden beim Anschluss ans Internet automatisch in einen Server hochgeladen.
Die Rohdaten des Smartphones wurden 1:1 in Exploration- sowie Validierungsdatensatz aufgeteilt und mittels des Statistikprogramms „statistics in R“ bearbeitet.

Ergebnis

Mehrere neu berechnete Parameter wurden im Explorationsdatensatz untersucht und im Validierungsdatensatz bestätigt. Die durchschnittliche Summe der Achsenzählung (sumXYZ) und die Varianz des durchschnittlichen Vektorenbetrags (varVM) konnten die unter Laborbedingungen durchgeführten körperlichen Aktivitäten gut unterscheiden und nahmen mit der Intensität der Aktivitäten zu. Bei der Identifizierung der Tragezeit zeigte varVM (AUC = 0.984, $p < 0.001$) eine höhere Sensitivität (0,987), Spezifität (0,941) sowie Genauigkeit (0,975) als sumXYZ und wurde für Tragezeitidentifizierung ausgewählt. In dieser Studie wurde also erstmalig ein neuer Parameter varVM, die Varianz des Vektorbetrags, eingesetzt. Der Vorteil dieses Parameters ist es, die Bewegungsveränderungen unabhängig der Lage des Smartphones zu messen.
Insgesamt liegen vollständige Daten von 138 Probanden, darunter 70 gesunde und 35 MS-Betroffenen mit progredientem und 33 mit schubförmigem Verlauf vor. Zwischen Gesunden und Betroffenen zeigte sich keinen signifikanten Unterschied bezüglich des Alters, der Geschlechtsverteilung, des Bauchumfangs sowie des BMIs. Die Betroffenen mit progredientem Verlauf waren älter als die mit dem schubförmigen Verlauf (49,6 vs. 35,9, $p < 0,05$).
Die durchschnittliche Tragezeit des Smartphones beträgt 55 Stunden (7,5 Stunden/Tag) und die des ActiGraphs 76 Stunden (10,9 Stunden/Tag).
Beim direkten Vergleich zwischen dem Smartphone (varVM) und dem ActiGraph (steps/minute) zeigte sich eine moderate Korrelation ($r = 0,44$, $p < 0,001$) unter allen Probanden, eine moderate Korrelation unter den gesunden Probanden ($r = 0,478$, $p < 0,001$) und eine schwache Korrelation unter den MS-Betroffenen ($r = 0,29$, $p = 0,022$).
Das Smartphone (varVM) zeigte eine höhere Assoziation zu den klinisch erhobenen Daten als das ActiGraph (steps per minute). Das Smartphone korrelierte unter allen Probanden mit fast

allen klinisch erhobenen Daten (Alter, Bauchumfang, alle klinischen Testen, GLTEQ und FAI, r = |0,21| bis |0,61|, p < 0,01). Innerhalb der Gesunden korrelierte das Smartphone mit den meisten klinischen Testen(2MWT, 6MWT, FTSTS, T25FW r = |0.21| bis |0.34|, p < 0.05). Innerhalb der MS-Betroffenen korrelierte das Smartphone mit den meisten klinisch erhobenen Daten (Alter, alle klinische Testen, GLTEQ, EDSS und MSWS, r = |0,37| bis |0,73|, p < 0,05).
Das ActiGraph korrelierte unter allen Probanden schwach mit den klinischen Testen und Fragebögen (r = |0.21| bis |0.34|, p < 0.05). Innerhalb der Gesunden und der MS-Betroffenen zeigte es sich keine Korrelation zwischen dem ActiGraph und den klinisch erhobenen Daten. Außerdem zeigten alle klinischen Testen einen signifikanten Unterschied zwischen den Gesunden und den MS-Betroffenen. Das Smartphone konnte den Unterschied besser als das ActiGraph widerspiegeln (AUC 0,75 vs 0,68).

Diskussion

In dieser Studie zeigte sich das Smartphone interessanterweise als eine zuverlässigere Messmethode als das wissenschaftlich angewandte ActiGraph, wenn es am Handgelenk getragen wird. Obwohl das Smartphone eine schwache Korrelation mit dem ActiGraph zeigte, assoziierte das Smartphone eindeutig stärker mit den klinischen Daten als das ActiGraph sowohl innerhalb der Gesunden als auch innerhalb der Betroffenen. Außerdem hat das Smartphone eine bessere Differenzierungsfähigkeit zwischen den Gesunden und den Betroffenen.
Ein anzunehmender Grund für die schwache Korrelation zwischen dem Smartphone und dem ActiGraph könnte die Trageposition des ActiGraphs sein. Obwohl das ActiGraph ein validierter Tool ist, wurde es in den meisten Studien an der Hüfte getragen[9,31,32] und die bisherigen Daten bezüglich der Trageposition am Handgelenk waren kontrovers[9,33–36]. In dieser Studie wurde das nicht dominante Handgelenk aufgrund der wahrscheinlich höheren Akzeptanz[35] als die Trageposition des ActiGraphs bestimmt. Die zusätzlichen Armbewegungen könnten während der relativ hohen Tragezeit des ActiGraphs die Messung der Gehfähigkeit verfälscht haben, während das Smartphone wahrscheinlich meistens nur dann bewegt wurde, wenn der Benutzer sich räumlich bewegte. Schließlich könnten die gewöhnlichen Trageposition eines Smartphones, z.B. in der Handtasche, im Rucksack oder in der Hosentasche, von Vorteil sein, weil die genannten Positionen sich näher am Zentrum der Körpermasse befinden und somit die realen Bewegungen beim Gehen besser gemessen werden könnten[36–38].

Unter den Korrelationen zwischen dem Smartphone und den klinischen Daten, ist die Assoziation zum Alter hervorzuheben. Das Alter ist bekanntlich ein allgemeiner Indikator für die körperliche Fitness und die Gehfähigkeit. Interessanterweise besteht zwischen dem Alter und dem Smartphone bei sowohl Gesunden als auch MS-Betroffenen eine moderate Korrelation ($r= -0,427$ und $-0,631$, $p < 0,0001$), während das ActiGraph nicht mit dem Alter korrelierte. Dies spricht für eine Smartphone-basierte Messung.

Beim genaueren Betrachten der Korrelationen zwischen dem Smartphone und den klinischen Daten fällt auf, dass der Smartphone-Parameter eine deutlich stärkere Assoziation hatte, zu den klinischen Testen sowie zu MSWS-12, die die Gehfähigkeit evaluieren, als zu den Fragebögen, die die körperliche Aktivität erfassen. Vermutlich misst das varVM eher die Gehfähigkeit als das körperliche Aktivitätsniveau. Es könnte daran liegen, dass das Smartphone während des Sports beiseitegelegt wird und somit die moderaten bis intensiven Körperlichen Aktivitäten nicht erfassen können. Diese Annahme bedarf weitere Untersuchungen.

Das Smartphone-Akzelerometer scheint, eine große Chance für ambulante Messung für MS-Betroffenen und generell neurologische Betroffenen mit Gehbehinderung zu sein. Es könnte den Ärzten helfen, die Gangdysfunktion, den Krankheitsverlauf sowie die Rehabilitation mit hoher ökologischer Validität zu verfolgen. In Hinsicht auf die Wechselbeziehung zwischen der Gehfähigkeit und der körperlichen Aktivität, wurde von unserer Arbeitsgruppe eine Patienteninformationsapp (PIA) entwickelt, die Bewegungswerte anzeigt und Informationen über Fitness und MS-Krankheit liefert, um die Betroffenen zu mehr körperlicher Aktivität zu motivieren. Dadurch könnten sich wiederum der Allgemeinzustand und die Gehfähigkeit weiter steigern. Die randomisierte Pilot-Studie mit der App[39] konnte zeigen, dass die MS-Betroffenen, die die App benutzt haben, eine höhere Bereitschaft hatten, ihren Lifestyle aktiver zu gestalten.

In der Auswertung der Rohdaten eines Smartphone-Akzelerometers steckt noch viel Potenzial. Datensätze mit kürzerem Zeitintervall als 60 Sekunden könnten zu mehr Genauigkeit führen. Durch maschinelles Lernen ist es denkbar, dass die Bewegungsdaten in Körperaktivitäten klassifiziert werden können, um das körperliche Aktivitätsniveau genauer zu bestimmen. Durch eine individuelle Auswertung der Bewegungsdaten könnte ein für jeden Benutzer angepasster Algorithmus errechnet werden. Dadurch könnte die Messung bei den Betroffenen mit neurologischen Defiziten, die mit abweichendem Bewegungsmuster und erhöhtem Energieverbrauch einhergehen, genauer sein.

Zusammenfassend konnte in dieser Studie mit einem neuen Parameter varVM gezeigt werden, dass das varVM als ein vielversprechendes Outcome in klinischen Studien und zur Verlaufsdokumentation eingesetzt werden kann. Gleichzeitig bietet das Smartphone eine zuverlässigere Messung der Gehfähigkeit als ein am Handgelenk getragenes ActiGraph im Alltagskontext für sowohl Gesunde als auch für MS-Betroffene.

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III. Zusammenfassung

Englische Version:

Based on the technical validation, we found the variance of the vector magnitude as a reliable estimate to discriminate wear time and no wear-time of the smartphone. Due to a further association with different activity levels, it was selected for real-life analyses. In the cross-sectional study, 67 pwMS and 70 matched controls underwent mobility tests and surveys. Real-life data were collected with a smartphone and an wrist worn ActiGraph over seven days. ActiGraph (steps per minute) correlated moderately ($r = 0.43$, $p < 0.05$) with the smartphone (varVM) but less with clinical tests (rho between |0.211| and |0.337|, $p < 0,05$). Smartphone data showed stronger correlations with age (rho = -0.487) and clinical tests (rho between |0.565| and |0.605|). ActiGraph only differed between pwMS and controls ($p < 0.001$) but not between disability groups. At the same time, the smartphone showed differences between pwMS and controls and between participants with and without ambulatory impairment (all $p < 0.001$).

Smartphone accelerometry provides better estimates of mobility and disability than a wrist-worn standard accelerometer in a free-living context for both controls and pwMS. Given the fact that no additional device is needed, smartphone accelerometry might be a convenient outcome of real-life ambulation in healthy individuals and chronic diseases such as MS.

Deutsche Version:

In der technischen Validierung wurde für den Smartphone-Bewegungssensor ein neuer Parameter varVM, Varianz des Vektorbetrags, eingesetzt. Es zeigte eine hohe Sensitivität (0,987), Spezifität (0,941) und Genauigkeit (0,975) für die Identifizierung der Tragezeit. Das varVM konnte körperliche Aktivitäten gut unterscheiden und nahmen mit der Intensität der Aktivität zu. In der Querschnittsstudie rekrutierten wir 67 MS-betroffene und 70 gesunde Probanden, bei den klinische Untersuchungen durchgeführt und Fragebögen erhoben wurden. Die Bewegungsdaten der Probanden wurden über 7 Tage von einem Smartphone sowie von einem am Handgelenk getragenen ActiGraph gesammelt. Das ActiGraph (steps per minute) korrelierte moderat mit dem Smartphone (varVM) ($r = 0,43$, $p < 0,05$) aber weniger mit den klinischen Untersuchungen (r zwischen |0,211| und |0,337|, $p < 0,05$). Das Smartphone korrelierte stärker mit dem Alter (r = -0,487) und den klinischen Untersuchungen (r zwischen |0,565| und |0,605|). Das ActiGraph konnte MS-Betroffene von den Gesunden unterscheiden

($p < 0{,}001$) während das Smartphone zwischen MS-Betroffenen und Gesunden sowie zwischen Betroffenen mit und ohne Gehbeeinträchtigung unterscheiden konnte ($p > 0{,}001$). Das varVM kann als ein vielversprechendes Outcome in klinischen Studien und zur Verlaufsdokumentation eingesetzt werden. Gleichzeitig bietet das Smartphone eine zuverlässigere Messung der Gehfähigkeit als ein am Handgelenk getragenes ActiGraph im Alltagskontext für sowohl Gesunde als auch für MS-Betroffene.

IV. Erklärung des Eigenanteils an der Promotion

Hiermit versichere ich, **Yuyang Zhai**, dass ich die folgenden Anteile für die Erstellung der Publikationspromotion „Validierung des Smartphone-Akzelerometers für die Messung der Gehfähigkeit sowie der körperlichen Aktivität im Alltagskontext unter MS-Betroffenen und Gesunden“ selbständig erarbeitet habe:

- Promotionsskizze
- Datenerhebung in Zusammenarbeit mit der Doktorandin Navina Nasseri und mit der studentischen wissenschaftlichen Hilfskraft Lilja Gutmann
- Deskriptive sowie statistische Datenauswertung in Zusammenarbeit mit Dr. Jan-Patrick Stellmann, Hilfsstellung
- Literaturrecherche und -auswertung
- Erstentwurf und Bearbeitung des Manuskripts

V. Danksagung

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VI. Lebenslauf

Lebenslauf wurde aus datenschutzrechtlichen Gründen entfernt.

VII. Eidesstattliche Versicherung

Ich versichere ausdrücklich, dass ich die Arbeit selbständig und ohne fremde Hilfe verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die aus den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen einzeln nach Ausgabe (Auflage und Jahr des Erscheinens), Band und Seite des benutzten Werkes kenntlich gemacht habe.
Ferner versichere ich, dass ich die Dissertation bisher nicht einem Fachvertreter an einer anderen Hochschule zur Überprüfung vorgelegt oder mich anderweitig um Zulassung zur Promotion beworben habe.
Ich erkläre mich einverstanden, dass meine Dissertation vom Dekanat der Medizinischen Fakultät mit einer gängigen Software zur Erkennung von Plagiaten überprüft werden kann.

Unterschrift: .....