An Objective Technology-based Assessment of Arm and Hand Sensorimotor Disability in Neurological Disorders

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Abstract

Background. Detailed assessments of upper limb disability are essential to understand and monitor sensorimotor recovery. Usually, multiple time-consuming assessments are required to define a holistic *sensorimotor profile* of proximal (shoulder-elbow) and distal (wrist-hand) impairments and their impact on the capacity to perform activities. We propose and evaluate a novel physiologically-motivated computational framework for objectively assessing sensorimotor profiles in neurological patients using a single, rapid technology-based assessment involving goal-directed arm and hand movements. *Methods.* The Virtual Peg Insertion Test (VPIT) was administered to 121 healthy and 80 neurological subjects. The framework provides 25 kinematic and kinetic metrics expected to describe 12 sensorimotor components representative of ataxia and paresis and their influence on task performance, as well as one overall disability measure. The feasibility (protocol duration), structural validity (factor analysis and correlations ρ between sensorimotor components), concurrent validity (correlation with Action Research Arm Test; ARAT), and discriminant validity (comparing healthy controls and patients, and patients with different disability levels) were evaluated. *Results.* The median VPIT protocol duration was 16.5min in neurological patients. The sensor-based metrics could unambiguously be grouped into 12 mostly independent (median $|\rho|=0.14$) components. Ten components showed significant differences between healthy and impaired subjects and nine components indicated clear trends across disability levels, without any ceiling effects. The VPIT overall disability measure

and ARAT were moderately correlated (ρ=−0.53, p<0.001). *Conclusions.* This work demonstrates the possibility to rapidly, holistically, and objectively assess proximal and distal sensorimotor impairments and their influence on the capacity to perform activities with a single assessment.

1 Introduction

The ability to plan and perform upper limb (UL) movements, involving the control of distal (wrist-hand) and proximal (shoulder-elbow) joints, is essential for successfully executing goal-directed activities, thereby influencing independence and quality of life.[1] Upper limb deficits are frequently observed in neurological disorders such as stroke, multiple sclerosis (MS), and hereditary ataxic conditions.[2–4] The neurological damage caused by the disorders is reflected in patient-specific *sensorimotor profiles* of UL disability. These profiles can be scientifically described using the computation, anatomy, and physiology (CAP) model[5] that translates into the clinically-oriented syndromes of ataxia and paresis.[6] Leveraging both concepts allows to connect abnormal movement behaviour, such as inefficient and non-smooth movements, dysmetria, impaired grasping control, weakness, and pathological muscle synergies, to their neurological cause, including inappropriately scaled motor commands and an inability to activate spinal motor neurons.[6]

A detailed assessment of sensorimotor profiles can help to better understand mechanisms underlying sensorimotor recovery and to evaluate novel interventions.[7,8] In clinical practice, holistic sensorimotor profiles are constructed by applying multiple clinical assessments that focus on proximal or distal joints (e.g., shoulder-elbow[9] or hand[10]) and the body function[9] or activity domain[10–12] of the International Classification of Functioning, Disability, and Health (ICF).[13] Applying such a battery of tests can be time-consuming,

with a single assessment taking up to 30min,[14] and outcome measures are often subjective, subject to floor and ceiling effects,[9] and have low sensitivity.[15]

Instrumented assessments promise to overcome these limitations by providing objective measures, which can be sensitive and valid biomarkers for sensorimotor recovery.[16–19] Existing technology-based assessments (e.g., using robotic devices such as the KINARM,[17] MEMOS,[20] and MIT-MANUS[18,21]) focus primarily on proximal arm impairments (ICF body functions) and do not analyze the coordination of distal and proximal movements.[8] This is, however, required for assessing the capacity to perform goal-directed activities (ICF activities) and, thereby, to create a holistic sensorimotor profile. The Virtual Peg Insertion Test (VPIT)[22] is a dedicated technology-based assessment with a goal-directed manipulation task combining distal and proximal UL movements. This approach aims to provide a detailed and rapid evaluation of UL disability (ICF body functions and activities) with a single test. The feasibility of the VPIT has been successfully tested in pilot studies with healthy subjects[23] and neurological patients.[22,24-26] However, a computational framework providing a complete and objective assessment of sensorimotor profiles based on kinematic and kinetic data still needs to be defined. Such a framework requires the definition of data processing steps and also the expected pathophysiological interpretation and structure (i.e., interdependency) of the proposed assessment metrics. This has been defined for clinical assessments,[27–29] but remains challenging for instrumented tools as different hypotheses and results were reported,[8,17,20,30] which renders the correct interpretation of many sensor-based metrics unclear.[8]

The objective of this work is to present a physiologically-motivated computational framework that enables the assessment of UL sensorimotor profiles in neurological

patients with one goal-directed task and to validate the approach in different populations (healthy, stroke, MS, hereditary ataxia). We hypothesized that (1) the proposed framework could extract multiple sensorimotor components that describe ataxia and paresis (ICF body functions). We additionally expected (2) that a combined *overall disability* measure would correlate to clinical assessments related to the ICF activity domain, (3) that the sensorimotor components are sensitive to differences between healthy and neurological populations, and (4) that they reveal trends across levels of disability. Establishing such a framework and its pathophysiological correlates is important, as it could help providing a fine-grained, objective, and insightful fingerprint of a neurological patient, thereby paving the way for the integration of single-task based technological assessments in research studies and clinical routine.

2 Methods

2.1 Participants

This work builds on data from different studies that used the VPIT as an outcome measure.[26,31] One-hundred-twenty-one healthy subjects (age 20-80 years) were recruited to provide age-matched control data. Additionally, 45 post-stroke subjects, 27 MS patients, and 8 patients with autosomal-recessive-spastic-ataxia of Charlevoix-Saguenay (ARSACS) were tested. Clinical assessments included the Fugl-Meyer upper extremity (FMA-UE)[9] and the Action Research Arm Test (ARAT)[11] for stroke patients, the ARAT, the Expanded Disability Status Scale,[32] and Fahn's Tremor Rating Scale (FTRS)[33] for MS patients, and the Nine Hole Peg Test (NHPT)[10] for ARSACS patients. Exclusion criteria

and ethical approval numbers are listed in the supplementary material (SM). All subjects gave informed consent.

2.2 Virtual Peg Insertion Test

The VPIT is an instrumented assessment combining a commercial haptic end-effector (PHANTOM Omni/Touch, 3D Systems, CA, USA), a custom-made handle with force sensors (CentoNewton40, EPFL, Switzerland) and a virtual reality (VR) environment (Figure 1a). The assessment features a goal-directed pick-and-place task that involves gross and fine UL movements while actively lifting the arm against gravity, thereby combining elements of the NHPT and the Box and Block Test.[10,12]

The task requires the successful transport of nine virtual pegs into corresponding holes by coordinating arm, hand, and cognitive function (details in previous work[22] and SM). The end-effector provides haptic feedback to render the virtual pegboard and holes to ease the perception of the 3D-space. During the execution of the task, 3D-end-point position, grasping forces, and interaction forces with the VR environment are recorded at 1kHz.

Participants were seated in a chair with backrest and without armrests in front of a personal computer with the haptic device being placed on the side of the tested limb. The initial position of the subjects (i.e., hand resting on the handle) was defined by a shoulder abduction angle of ~45°, a shoulder flexion angle of ~10°, and an elbow flexion angle of ~90°. Subjects were familiarized with the task and subsequently performed five repetitions (i.e., inserting all nine pegs five times) per body side (details in previous work).[24] Participants were instructed to perform the task as fast and accurately as possible.

2.3 Data preprocessing

Raw signals were low-pass filtered using a zero-phase Butterworth filter (2nd order, cut-off frequency 10Hz; Figure 1b). Movement and haptic trajectories were segmented into the *approach* (i.e., from reaching 1cm distance to the current peg until lifting that peg), *transport* (i.e., from lifting a peg until reaching 2cm distance of the targeted hole), and *return* (i.e., from inserting a peg until approaching the next peg) phases. Grasping force trajectories were segmented into the *force buildup* (i.e., behaviour during maximal production of force) and *force release* phases (i.e., behaviour during maximal release of force; see SM and Figure SM2).

2.4 Sensorimotor profiles and assessment metrics

We defined a sensorimotor profile as a combination of 12 physiologically-motivated sensorimotor components and one *overall disability* measure, which are built on 25 metrics extracted from VPIT data. In the following, a description and motivation for the proposed sensorimotor components is presented by considering the CAP model[5] and the clinical syndromes ataxia and paresis.[6] Metrics (details in Table SM1 and Eq. SM4-SM18) were preselected based on an extensive literature review,[8,30] preliminary validity and reliability results, and the technical and clinical experience of the authors. The proposed hypotheses regarding the interpretation of metrics and components are later used for analyzing structural validity.

2.4.1 Movement smoothness/efficiency

Two commonly used paradigms for the analysis of movement quality are *smoothness* and *efficiency*.[34,35] Goal-directed movements are executed by translating parameters such as target distance into neural commands of certain amplitude, which are transferred to peripheral muscles performing the movement.[6] The signals' amplitude is chosen to minimize movement endpoint variance, which leads to smooth behaviour (i.e., bell-shaped velocity trajectories).[36] These velocity trajectories can be modeled using a superposition of submovements and minimize the magnitude of the jerk trajectory.[35] In neurological subjects, more submovements with increased temporal shift and higher jerk magnitudes[37,38] have been observed, potentially due to disrupted feedforward mechanisms. During neurorehabilitation, the temporal shift between subcomponents and the jerk magnitude reduced,[37] thereby highlighting their relevance to track recovery.

Furthermore, a trade-off between speed and accuracy was described by Fitt's law[34] and is imposed through velocity-dependent neural noise.[36] Previous studies suggested that neurologically impaired subjects tend to follow a trajectory that is less close to the optimal trajectory compared to healthy controls[39] and that this behaviour correlates with impairment severity.[19] This suboptimal *movement efficiency* could result from erroneous state estimates for feedforward control but also from weakness.[6]

In our application, we hypothesized that *smoothness* and *efficiency* are directly related and used three metrics to jointly represent both constructs. First, the integrated jerk normalized with respect to movement duration and length should represent the intrinsic minimization of jerk.[37] Second, the spectral arc length of the velocity trajectory should reflect energy induced by jerky movements.[16] Third, the path length ratio (i.e., shortest

possible distance divided by actually covered distance) should represent inefficient movements. We calculated these metrics separately for *transport* and *return* as only the *transport* requires precise grip force control, which could further affect feedforward control mechanisms.

2.4.2 Movement curvature

Goal-directed movements in healthy subjects tend to follow a trajectory similar to the shortest path between start and target.[40] In post-stroke patients, increased *movement curvature* (i.e., increased deviation from the straight line) was observed,[39] which can result from disrupted feedforward control[41] and from an abnormal flexor synergy pattern when performing shoulder flexion and abduction.[39] While this abnormal flexor synergy pattern is not commonly observed in patients with MS or ARSACS, we expected movement curvature to be a possible indicator of disrupted feedforward control or weakness in these patients.

We selected three metrics to analyze the deviation from the optimal trajectory in the horizontal plane to detect movements close to the trunk. The angle between actual and optimal trajectory was estimated when 20% of the total distance was reached.[41] Additionally, the mean and maximal trajectory error with respect to the ideal, straight trajectory were calculated.[24] These metrics were extracted separately for *transport* and *return* as we expected differently pronounced synergistic movements during elbow flexion and extension.[42]

2.4.3 Movement planning

Healthy, ballistic movements are planned and executed in a feedforward manner. This behaviour can be disrupted due to incorrectly scaled neural commands in ataxic patients.[6,32] To evaluate higher order *movement planning*, we analyzed spatio-temporal aspects of distorted feedforward control, which assumes that peak velocity occurs at approximately 50% of the covered distance for an ideal bell-shaped movement. We hypothesized that the planning behaviour differs between *transport* and *return*. Therefore, we calculated the distance covered at peak velocity normalized with respect to the totally covered distance for both phases individually.[17]

2.4.4 Endpoint error

An under- or overshoot when reaching for a target, referred to as dysmetria, can result from inappropriately scaled motor commands and thereby disrupted feedforward control,[36] but also cognitive and proprioceptive deficits.[43] Dysmetria was observed in post-stroke patients with lateral-posterior thalamic lesions,[43] is a common manifestation of intention tremor in MS,[44] and is typically present in patients with cerebellar ataxia.[45] In the VPIT, the maximal Euclidean distance between 2D horizontal cursor and peg position during the peg *approach* phase was calculated to represent dysmetria.

2.4.5 Dropped pegs

The number of dropped pegs describes how often the grasping force dropped below a 2N threshold while lifting a virtual peg.[24] We hypothesized that the metric describes the control of grasping forces and potentially also the coordination of proximal and distal movements.

2.4.6 Grip force scaling and force buildup/release control

Increased safety margins during object manipulations and decreased force control have been reported in neurological patients and were attributed to distorted somatosensory feedback and processing.[46–51] Also, a reduction in applied grip force levels (*force scaling*) due to weakness might be expected depending on a patients' neurological profile.[6] While the ability to produce and maintain submaximal grip forces has been shown to be preserved,[48] a slowness of *force buildup*[47] and *force release*[48] has also been reported. Additionally, there is evidence suggesting that force control is a separate entity to grip strength,[48,49] that *force buildup* and *release* have different neural mechanisms,[48] and that force control can further be decomposed into *force scaling* and motor coordination.[49]

We extracted six metrics to describe *force scaling*, *force buildup control*, and *force release control*, which we hypothesized to be independent components. To describe *force scaling*, we calculated the maximal absolute force rate during the *force buildup* and *force release* phases. For quantifying *force buildup control*, we estimated the duration of the *force buildup* phase. Additionally, we estimated the spectral arc length of the force rate profile during the *force buildup* phase to capture smoothness of *force buildup*. Analogous

to the metrics describing *force buildup control*, we calculated the same metrics during the *force release* phase (Figure SM2).

2.4.7 Haptic collisions

Haptic collisions describe the interaction forces between the subject and the virtual pegboard rendered through the haptic device. Haptic guidance can be used to ease inserting the virtual pegs into the holes, which have reduced haptic impedance. Previous studies indicated increased haptic collisions forces in multiple neurological disorders[52] and especially stroke patients with sensory deficits.[22] We additionally hypothesized that collision forces during *transport* and *return* (i.e., phases during which haptic guidance is not required) could be increased due to arm weakness. In particular, neurological patients can have a limited capability to lift their arm against gravity,[42] leading to increased vertical *haptic collisions*. We expected pathological behaviour to be similar during *transport* and *return* as sensory deficits and gravity-related weakness might not be selective to a specific movement phase. The mean vertical collision force was calculated during *transport* and *return* to quantify *haptic collisions*.

2.4.8 Overall disability

A single indicator describing the patient-specific *overall disability* level was defined as a combination of the previously defined components and the *task completion time*.

2.5 Data postprocessing

To reduce the influence of intra-subject variability, the grand mean across pegs and repetitions was estimated for each metric, which were subsequently expressed as percentiles relative to the distribution of an age-matched healthy *reference population* with the goal to standardize the range of all metrics to the interval]0,100[. This simplifies their physiological interpretation and allows to aggregate multiple metrics describing the same sensorimotor component, thereby enabling a robust analysis and dimensionality reduction. The *reference population* was tailored to the currently analyzed individual patient or population based on the age and tested body side. For analyzing single subjects, data points (N: successful completion of the VPIT protocol with one body side) in the *reference population* with an age within the analyzed subject ±5 years were selected. When analyzing populations, subjects in the *reference population* with an age within the range of the analyzed population were selected. Continuous cumulative density functions (CDF) were estimated for each metric based on the *reference population* using kernel density estimation. For each analyzed subject, the value of a metric was expressed as percentile of the *reference population* while considering the theoretical optima and pessima (i.e., physiologically-motivated hypotheses) of each metric (Figure SM1, Figure SM4, Table SM1). Subsequently, an *arcsin* transformation was applied to optimize the sensitivity of the CDFs. Lastly, a single indicator per sensorimotor component was obtained by aggregating the metrics belonging to this component using the root mean square operation. Details can be found in the SM.

2.6 Data analysis

Clinical feasibility was analyzed with the VPIT protocol duration (i.e., including patient setup, instructions, five repetitions of the test, and resting periods) with the most-affected body side (data available for 14 stroke, 18 MS, and 8 ARSACS patients).

To establish the pathophysiological correlates and structural validity of the sensor-based metrics, a confirmatory factor analysis (CFA) and correlation-based interdependence evaluation was performed for all healthy and neurological subjects. For the CFA, the number of factors was set to k=12 based on the stated hypotheses. Outcome measures of the CFA were the loadings of each metric on each factor, with an absolute loading value of at least 0.50 indicating a strong loading.[53] Additionally, Spearman correlation coefficients evaluated the interdependence between the proposed sensorimotor components.

Concurrent and discriminant validity were analyzed with *specific data sets* using only the first available testing time-point and only subjects with available clinical data. Additionally, only data from the paretic limb were analyzed for stroke patients, which were subdivided into three groups according to their FMA-UE score (ceiling: FMA-UE=66; mild impairment: 54≤FMA-UE<66; moderate impairment: 35≤FMA-UE<54).[54] This was preferred over the grouping with the ARAT to analyze the relationship of the proposed approach with a measure of ICF body functions. For the MS and ARSACS population, data from both body sides were analyzed. MS subjects were split into three groups based on their ARAT score (full capacity: 55≤ARAT≤57; notable capacity: 43≤ARAT<55; limited capacity: 22≤ARAT<43).[28] ARSACS patients were divided into three different age-groups (young: 26≤age≤36; mid-age: 37≤age≤47; older-age: 48≤age≤58) due to the neurodegenerative nature of the disease.[4] Concurrent validity was analyzed in the

combined stroke and MS population using the Spearman correlation between the VPIT *overall disability* and the ARAT score. Discriminant validity was analyzed by comparing the sensorimotor profiles between the age-matched healthy and each patient population grouped according to the disability level. A Kruskal-Wallis omnibus test followed by Dunn's post-hoc tests was applied to check for statistically significant differences between groups. Bonferroni correction was applied whenever suitable. A cut-off of 85.6% (normalized VPIT score) corresponding to the established 95th-percentile cut-off was used to discriminate healthy and abnormal behaviour.[17] Further details can be found in the SM.

3 Results

Data from 121 healthy subjects (N=242) were used to create age- and side-matched *reference populations* for each analysis. For the CFA and interdependence analysis, 45 stroke patients (N=128), 27 MS patients (N=64), and 8 ARSCAS patients (N=16) were additionally used. An overview of the *specific data sets* used for discriminative and concurrent validity analysis can be found in Table 1.

The time to complete the VPIT protocol was 16.5min [11.2, 26.0; 10.0, 31.0] with the most-affected body side (median [25th-percentile, 75th-percentile; minimum, maximum]).

CFA coefficients (Table 2) showed strong loadings on the same factor for all metrics belonging to the defined sensorimotor component. The components of the sensorimotor profile showed zero very high, three high, zero moderate, 11 low, and 52 very low inter-correlations (Table 3; $|\rho|$=0.14 [0.06, 0.26]).

For illustrative purposes, movement and grasping force trajectories and resulting sensorimotor profiles were visualized for one representative healthy, stroke, MS, and ARSACS subject in Figure 2 (variability in Figure SM3).

The Spearman correlation between the VPIT *overall disability* and the ARAT score was -0.53 (*p*-value<0.001). Population-based sensorimotor profiles are presented in Figure 3 (*p*-values before/after Bonferonni correction in Table SM2). All sensorimotor components except *movement planning transport*, *force scaling*, and *haptic collisions* showed significant differences between healthy controls and at least one patient subpopulation. Similarly, all sensorimotor components except *force scaling* detected disability in single subjects based on the defined cut-off. Clear trends (i.e., monotonically increasing medians) across disability levels were observed across patient subgroups with increasing severity for all sensorimotor components except *movement curvature transport*, *movement curvature return*, *movement planning return*, and *force scaling*. These trends were statistically significant only for *endpoint error* in MS patients after Bonferonni correction.

4 Discussion

In this paper, we presented a physiologically-motivated computational framework for holistically assessing UL sensorimotor profiles in neurological disorders using a single technology-based assessment requiring arm and hand movements. The objective was to first motivate and define the framework and to evaluate its ability to assess sensorimotor disability (ICF body functions and activities) in 80 neurological patients with different severity levels. Based on the CAP model and the clinical syndromes ataxia and paresis,[5,6] we established the pathophysiological correlates of 25 sensor-based metrics that we grouped into 12 sensorimotor components and one *overall disability* measure. The components showed high independence, were able to discriminate controls and patients,

and could reveal trends across levels of disability. Additionally, the proposed *overall disability* measure correlated moderately with the ARAT (ICF activities) and allowed to quantify the influence of ataxia and paresis (ICF body functions) on the capacity to perform goal-directed activities. This evidence, in combination with an assessment duration considerably below the time required for a battery of clinical assessments,[9,14] highlights the ability to assess sensorimotor profiles in multiple neurological disorders with a single goal-directed manipulation task. Altogether, this work proposes a novel approach to exploit the benefits of sensor-based assessments in an accurate, efficient, and insightful manner.

4.1 Clinical relevance of the sensorimotor profiles

The VPIT provides a dedicated assessment platform tailored to patients with mild to moderate disability, as it requires residual hand function and active lifting of the arm against gravity. The experience gained from multiple clinical studies suggests that the VPIT is especially viable for patients with at most moderate UL impairments (e.g., FMA-UE score≥30) or limited capacity (e.g., ARAT≥22). This should be acknowledged as a possible limitation compared to other technology-based assessments that also target severely impaired patients.[17,20] However, these do not evaluate hand function, the coordination of grip forces during reaching, and the impact of impairments on the capacity to perform activities. Additionally, these platforms typically provide arm weight support, which can influence assessment outcomes and might lead to reduced validity.[23,55] Also, sensor-based assessment metrics are often extracted from robot-assisted therapy platforms,[18,20,21] which can be biased through therapy-related learning effects.[56] Similar concepts to the VPIT have been proposed, but were not able to quantify hand impairments[52,57,58] or had limited clinical feasibility.[59]

The possibility to assess UL sensorimotor disability has been thoroughly motivated and evaluated in a large population of healthy and neurological subjects. So far, such an effort has mainly been done for one other dedicated assessment platform, the KINARM, which allows a detailed assessment of sensorimotor arm impairments (e.g., visuomotor, sensorimotor, and proprioception) with a battery of instrumented tasks.[17] Our proposed approach complements this work by providing information about sensorimotor arm and hand impairments and their impact on the capacity to perform activities. Additionally, the structural validity of sensor-based metrics has only been investigated by one group, which was able to decompose proximal movements into three factors describing accuracy, smoothness, and velocity.[60] Our proposed approach therefore enables an evaluation that may contain more physiologically-relevant information. Further, the proposed data normalization procedure allows, for the first time, an intuitive interpretation and comparison of sensor-based metrics without artificially introducing ceiling and floor effects, thereby facilitating clinical integration and comparison of research studies.[9]

The proposed framework can overcome limitations of conventional clinical scales such as ceiling effects, as commonly reported in the FMA-UE and ARAT.[9,11] Evidence for this is provided by the high variability in the sensorimotor profiles of stroke and MS patients with highest FMA-UE and ARAT scores, respectively, as well as the significant differences between healthy subjects and MS patients with full capacity according to *movement smoothness/efficiency return*, *dropped pegs*, and the *overall disability score*. In addition, the fact that three sensorimotor components did not show trends across all levels of impairment severity might be explained by the use of a single clinical assessment for classifying impairment severity, which does not cover all components of the proposed sensorimotor profile. For example, *force scaling* did not show trends across stroke

patients with different disability level. However, these subjects were grouped according to the FMA-UE, which primarily focuses on proximal movement patterns and not hand control.[9] This underlines that the information content of the sensorimotor profiles goes beyond that of a single clinical assessment.

4.2 Pathophysiological correlates of the sensorimotor profiles

We were able to validate the interpretation of the metrics by confirming their unambiguous grouping into 12 factors describing mostly independent components of ataxia and paresis as well as their influence on activity capacity. Very high intercorrelations were only found between *movement smoothness/efficiency transport*, *movement smoothness/efficiency return*, and *dropped pegs*. Nevertheless, it is likely that these components still assess different pathophysiological aspects and that, instead, the neurological damage affects these constructs in a similar way. This is supported by the correlation within the former and the latter two components that is likely not causative considering the test design (i.e., different requirements for feedforward control during *transport* and *return*; pegs cannot be dropped during *return*). However, we cannot rule out that dropping a peg during *transport* mathematically implies reduced *movement smoothness/efficiency transport*.

Further, the individual-level results allowed to relate specific sensorimotor components to ataxia and paresis, as the movement patterns observed in kinematic and kinetic trajectories of representative patients were objectively reflected in their sensorimotor profiles and clinical scores (Figure 2). For example, the stroke patient performed movements that were smooth and symmetric, but mostly executed closer to the trunk than observed in healthy subjects. This pattern might be characteristic of an abnormal flexor synergy, which is potentially present in this patient according to clinical

observations and the FMA-UE score (43/66). This behaviour was quantitatively reflected in the sensorimotor profile, which indicated *movement smoothness/efficiency* similar to healthy subjects but *movement curvature* deviating from healthy behaviour. This patient also applied grasping forces in an excessive manner, which might be related to somatosensory deficits that might also be reflected in deficits during object manipulations according to the ARAT score (13/57). The patient with MS showed a spatial overshoot when approaching the pegs, which was objectively captured by the sensorimotor profile showing increased endpoint error. This corresponded to clinical observations according to the FTRS that indicated a markedly abnormal dysmetria score (3/4). The ARSACS patient showed especially jerky movements deviating from the optimal trajectory, which can stem from reduced UL coordination.[26] The sensorimotor profile captured this behaviour and indicated impairment in *movement smoothness/efficiency*, *movement planning*, and *movement curvature*. Compared to the stroke patient, *movement curvature* might here be an indication of reduced coordination due to inappropriately scaled motor commands. These results provide first evidence that the sensorimotor components might be helpful to inform on feedforward/sensory mechanisms underlying movements, arm-hand coordination, grasping force scaling and control, arm weakness, and abnormal flexor synergy patterns and their impact on the capacity to perform goal-directed activities.

4.3 Limitations

We acknowledge that the hypotheses underlying the metrics require further validation, which could be achieved by comparisons with specific clinical scales. Further, the VPIT might be limited to patients without severe cognitive deficits, as subjects need to learn the

visuospatial transformation between end-effector and virtual cursor and need to perceive depth in the VR environment.

5 Conclusions

A framework to holistically and rapidly assess UL sensorimotor profiles using a single technology-based assessment requiring arm and hand movements was physiologically motivated and successfully evaluated. The proposed approach can be seen as a time-efficient and valid alternative to establish sensorimotor profiles describing ataxia and paresis (ICF body functions) and their impact on capacity (ICF activities). Future work will focus on analyzing clinimetrics, which can further support the integration of this approach into research studies and clinical routine.

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Tables

Table 1: **Participant demographics.** Subjects were split into three groups according to the FMA-UE, ARAT, and age for the stroke, MS and ARSACS population, respectively. Data from the most-affected side of stroke patients and both sides of MS, ARSACS, and healthy subjects was used. Only the first available time-point was used for each subject. A *data point* is defined as the successful completion of the VPIT protocol with one body side.

Demographics	**Healthy subjects**	**Neurologically impaired subjects**								
		Stroke			**MS**			**ARSACS**		
		Ceiling	Mild impairment	Moderate impairment	Full capacity	Notable capacity	Limited capacity	Young	Mid-age	Older-age
Subjects (n)	121	8	8	13	6	10	4	3	3	2
Data points (N)	242	8	8	13	11	16	4	6	6	4
Age *(yrs)*	50.72 (17.36)	51.23 (14.34)	54.03 (10.09)	64.78 (14.57)	49.36 (9.28)	51.69 (15.91)	56.5 (14.27)	28.67 (2.25)	38.33 (2.07)	57 (1.15)
Gender *(m/f)*	120/122	6/2	7/1	8/5	6/5	6/10	0/4	4/2	2/4	2/2
Hand dominance *(l/r)*	28/214	0/8	2/6	2/11	0/11	3/12	0/4	0/6	2/4	2/2
Most affected side *(l/r)*	-	5/3	6/2	7/6	6/4*	6/9*	1/3	-	-	-
Chronicity *(yrs)*	-	0.31 (0.34)	0.29 (0.34)	0.06 (0.07)	-	-	-	-	-	-
MS type *(PP/SP/RR)*	-	-	-	-	2/5/4	4/5/7	0/2/2	-	-	-
FMA-UE *(0-66)*	-	66 (0)	58.63 (4.37)	45.23 (5.4)	-	-	-	-	-	-
ARAT *(0-57)*	-	55.38 (3.42)	56.13 (1.73)	37.62 (16.03)	56 (0.63)	50.06 (3.68)	34.75 (4.35)	-	-	-
EDSS *(0-10)*	-	-	-	-	4.82 (1.29)	6.44 (1.28)	6.63 (1.11)	-	-	-
NHPT *(s)*	-	-	-	-				37.68 (14.62)*	37.2 (7.42)*	71.64 (21.71)

Abbreviations: I: Ischaemic. H: Hemorrhagic. CC: Cortical. SC: Subcortical. PP: Primary Progressive. SP: Secondary Progressive. RR: Relapse Remitting. EDSS: Expanded Disability Status Scale. FMA-UE: Fugl-Meyer Assessment for Upper Extremity. ARAT: Action Research Arm Test. NHPT: Nine Hole Peg Test. Reported as mean (standard deviation). *Information missing for one subject.

Table 2: **Structural validity of sensor-based metrics.** Loadings of metrics on underlying factors extracted using confirmatory factor analysis. Association of metrics to a certain sensorimotor aspect was physiologically motivated initially. Bold values indicate cross- or strong loadings (i.e., absolute loading of at least 0.32). Loadings are defined within [-1,1] with larger absolute values indicating a stronger contribution to a factor.

Sensorimotor aspect	**Sensor-based metric**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Movement smoothness/efficiency transport	Jerk transport	**0.47**	-0.01	-0.03	-0.02	0.02	0.00	-0.02	0.17	-0.01	0.05	0.01	0.01
	Spectral arc transport	**0.41**	0.09	-0.01	-0.04	0.00	0.00	0.02	0.06	-0.02	0.02	-0.01	0.04
	Path length ratio	**0.60**	0.00	0.04	-0.02	-0.01	0.01	0.00	-0.12	0.02	-0.04	-0.02	-0.04
Movement smoothness/efficiency return	Jerk return	0.13	**0.52**	-0.02	0.02	0.00	-0.03	-0.06	0.00	-0.01	-0.01	0.04	-0.06
	Spectral arc return	0.00	**0.63**	0.00	-0.01	-0.02	0.04	-0.06	-0.08	0.01	0.01	-0.02	0.05
	Path length ratio return	-0.02	**0.41**	0.00	0.08	0.03	-0.01	0.28	0.15	-0.01	-0.04	0.00	0.04
Movement curvature transport	Trajectory error transport	-0.02	-0.02	**0.64**	0.01	-0.01	0.00	-0.01	-0.06	-0.01	-0.01	0.02	0.01
	Trajectory error max transport	0.26	0.06	**0.42**	0.03	-0.03	0.02	0.02	-0.20	0.02	-0.01	-0.02	-0.04
	Initial movement angle transport	-0.11	-0.04	**0.64**	-0.01	0.03	-0.01	-0.01	0.17	-0.01	0.02	0.01	0.01
Movement curvature return	Trajectory error return	-0.16	-0.01	0.02	**0.64**	0.00	0.02	-0.01	0.13	-0.01	0.02	-0.03	-0.01
	Trajectory error max return	-0.06	0.19	0.04	**0.48**	0.03	0.00	0.02	-0.01	0.00	0.01	-0.04	-0.03
	Initial movement angle return	0.28	-0.23	-0.09	**0.58**	-0.04	-0.04	-0.02	-0.19	0.01	-0.03	0.10	0.05
Movement planning transport	Distance to max vel transport	0.02	-0.01	0.00	0.01	**0.99**	0.00	0.00	0.00	0.00	-0.01	0.00	0.00
Movement planning return	Distance to max vel return	0.01	-0.01	-0.01	0.01	0.00	**0.99**	0.00	-0.01	0.00	0.00	0.01	0.00
Endpoint error	Endpoint error return	0.01	-0.06	0.00	-0.02	-0.01	0.00	**0.96**	-0.03	0.00	0.01	0.00	-0.01
Dropped pegs	Dropped pegs	0.14	0.01	-0.01	0.03	-0.01	-0.01	0.00	**0.80**	0.02	0.00	0.01	-0.02
Force scaling	Force buildup max	-0.01	-0.03	0.00	-0.01	-0.02	0.01	0.01	0.03	**0.69**	-0.07	0.05	-0.01
	Force release max	0.00	0.02	0.00	0.01	0.02	-0.01	-0.01	-0.01	**0.72**	0.06	-0.05	0.01
Force buildup control	Force buildup spectral arc length	0.05	-0.11	0.01	0.01	-0.02	0.03	-0.02	0.21	-0.01	**0.66**	-0.02	0.01
	Force buildup duration	-0.01	0.08	-0.01	0.00	0.01	-0.03	0.02	-0.19	0.00	**0.73**	0.03	-0.01
Force release control	Force release spectral arc length	0.01	-0.06	0.01	0.00	-0.03	0.03	-0.02	0.19	-0.03	-0.06	**0.70**	0.02
	Force release duration	-0.04	0.10	0.00	-0.02	0.03	-0.03	0.02	-0.17	0.03	0.07	**0.70**	-0.02
Haptic collisions	Collision force mean transport	-0.10	0.11	0.00	0.03	-0.02	0.01	0.00	0.06	0.04	0.03	-0.03	**0.70**
	Collision force mean return	0.11	-0.10	0.00	-0.04	0.02	-0.01	0.00	-0.07	-0.04	-0.03	0.02	**0.71**

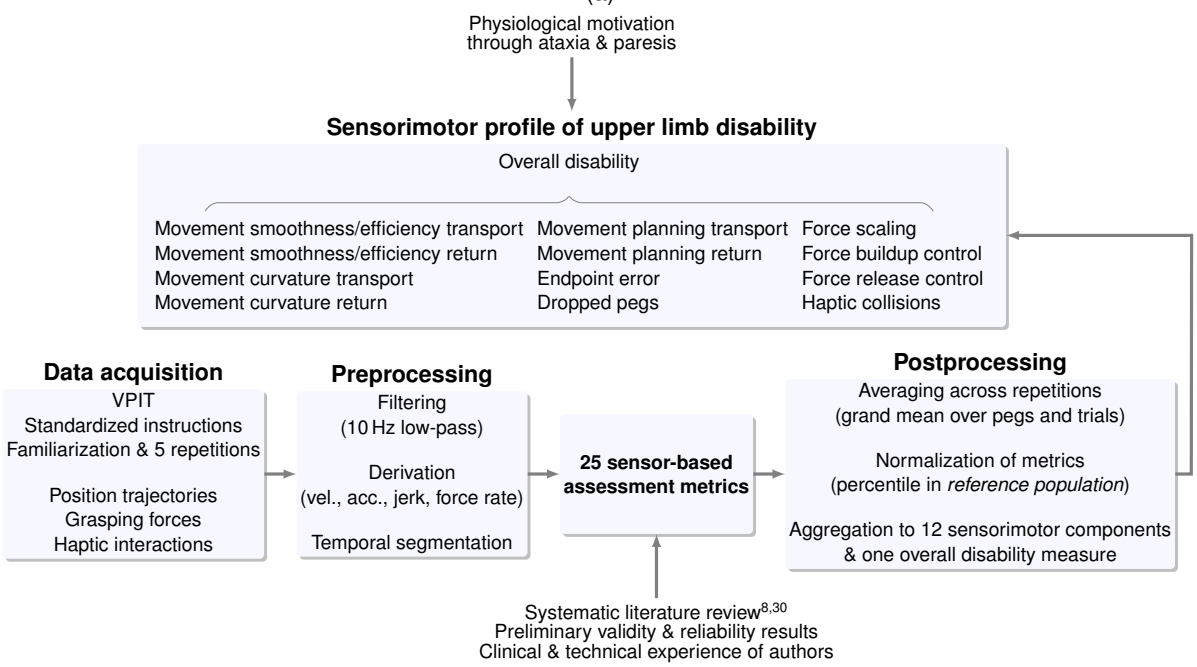
Abbreviations: F1-12: Factors 1-12 (sorted according to sensorimotor components).

Table 3: **Structural validity of the sensorimotor components.** Spearman correlations were calculated between the components of a sensorimotor profile. Sensorimotor components are a combination of sensor-based metrics with similar pathophysiological interpretation. Bold values indicate p-values below the significance level after Bonferroni correction. The Bonferroni significance level was 0.00076.

	Movement smoothness/efficiency transport	Movement smoothness/efficiency return	Movement curvature transport	Movement curvature return	Movement planning transport	Movement planning return	Endpoint error	Dropped pegs	Force scaling	Force buildup control	Force release control
Movement smoothness/efficiency return	**0.81**										
Movement curvature transport	**0.33**	**0.25**									
Movement curvature return	**0.26**	**0.26**	**0.33**								
Movement planning transport	**0.14**	**0.15**	0.10	0.02							
Movement planning return	**0.26**	**0.31**	0.09	0.10	0.10						
Endpoint error	**0.33**	**0.43**	0.06	0.06	0.04	**0.15**					
Dropped pegs	**0.74**	**0.71**	**0.16**	**0.14**	0.14	**0.18**	**0.30**				
Force scaling	0.05	0.02	0.08	0.05	0.07	0.02	0.07	0.04			
Force buildup control	**0.44**	**0.44**	0.06	**0.21**	0.01	0.10	0.07	**0.33**	-0.07		
Force release control	**0.29**	**0.33**	**0.19**	**0.17**	0.11	0.12	0.03	**0.19**	0.01	**0.41**	
Haptic collisions	**0.20**	**0.22**	-0.02	**-0.17**	0.00	0.00	**0.26**	**0.23**	0.06	0.06	0.08

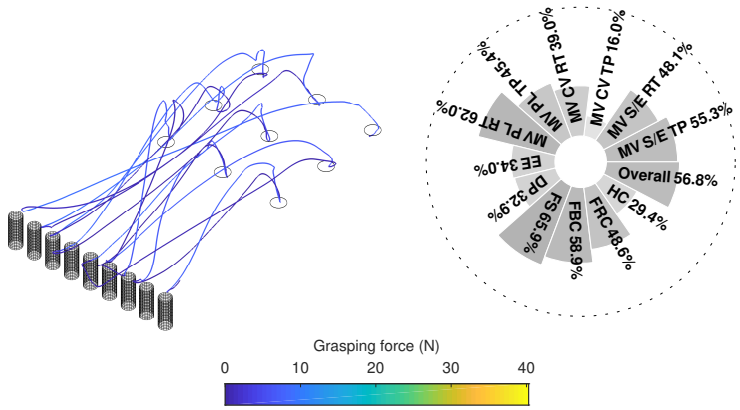
Figures

(a)

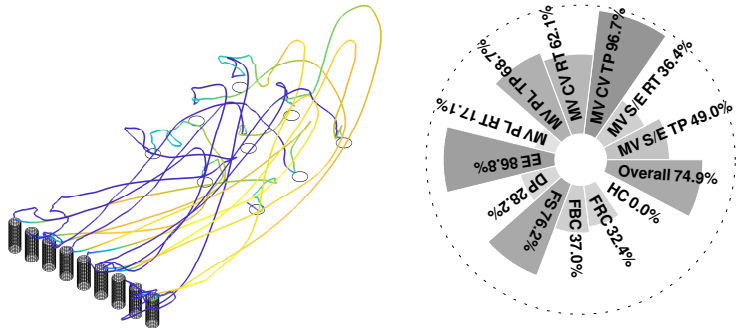


(b)

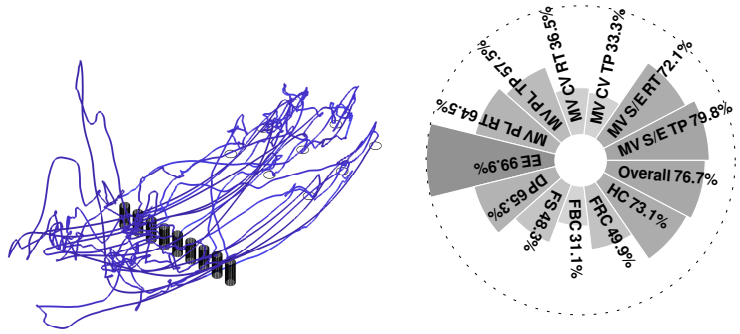
Figure 1: (a) setup of the Virtual Peg Insertion Test (VPIT), a technology-based assessment requiring arm and hand movements combining a commercial haptic device, a spherical handle instrumented with force sensors, and a virtual reality environment displaying a virtual pegboard. (b) overview of the physiologically-motivated computational framework to construct sensorimotor profiles of upper limb disability (ICF body functions and activity). Abbreviations: vel.: velocity. acc.: acceleration.



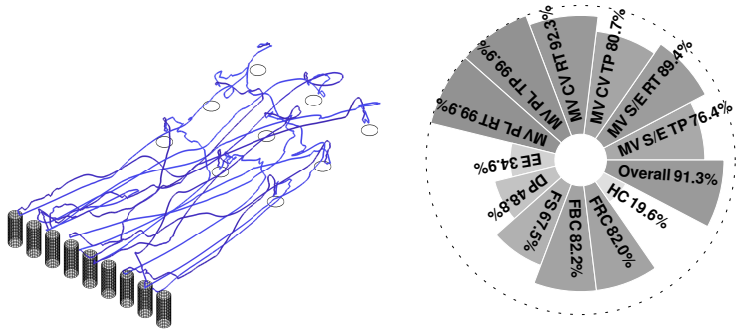
(a) Healthy subject (age 29 yrs, VPIT time 19.4 s)



(b) Stroke patient (age 74 yrs, FMA-UE 43, ARAT 13, VPIT time 51.8 s)

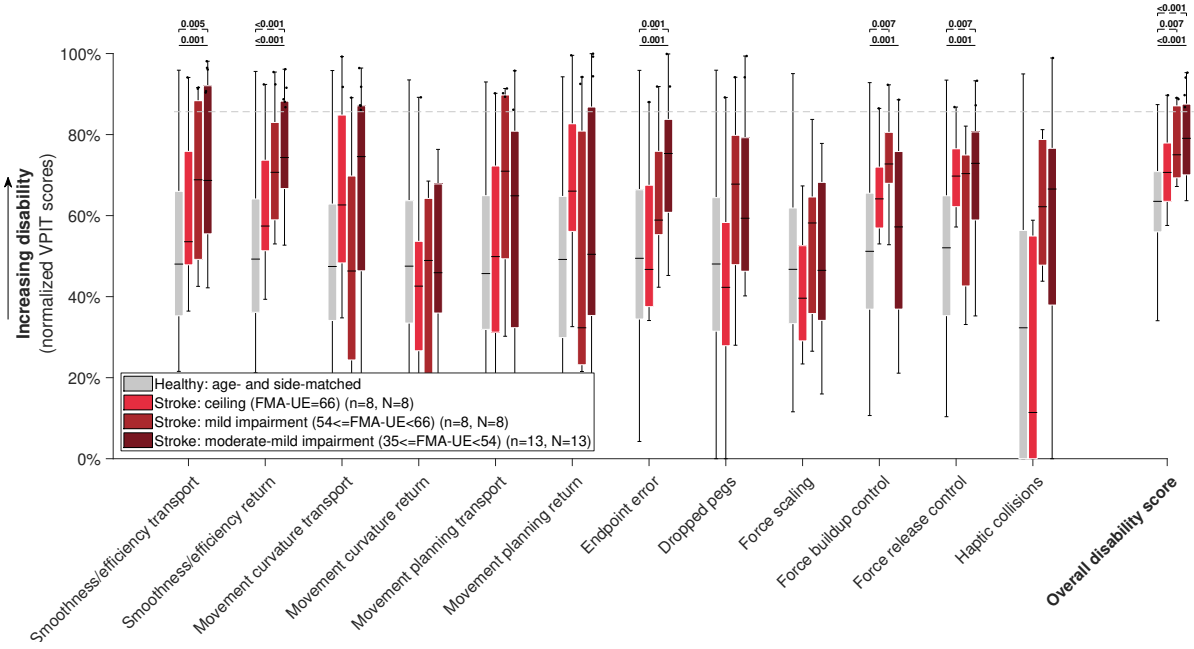


(c) MS patient (age 76 yrs, ARAT 34, FTRS dysmetria 3, VPIT time 97.2 s)

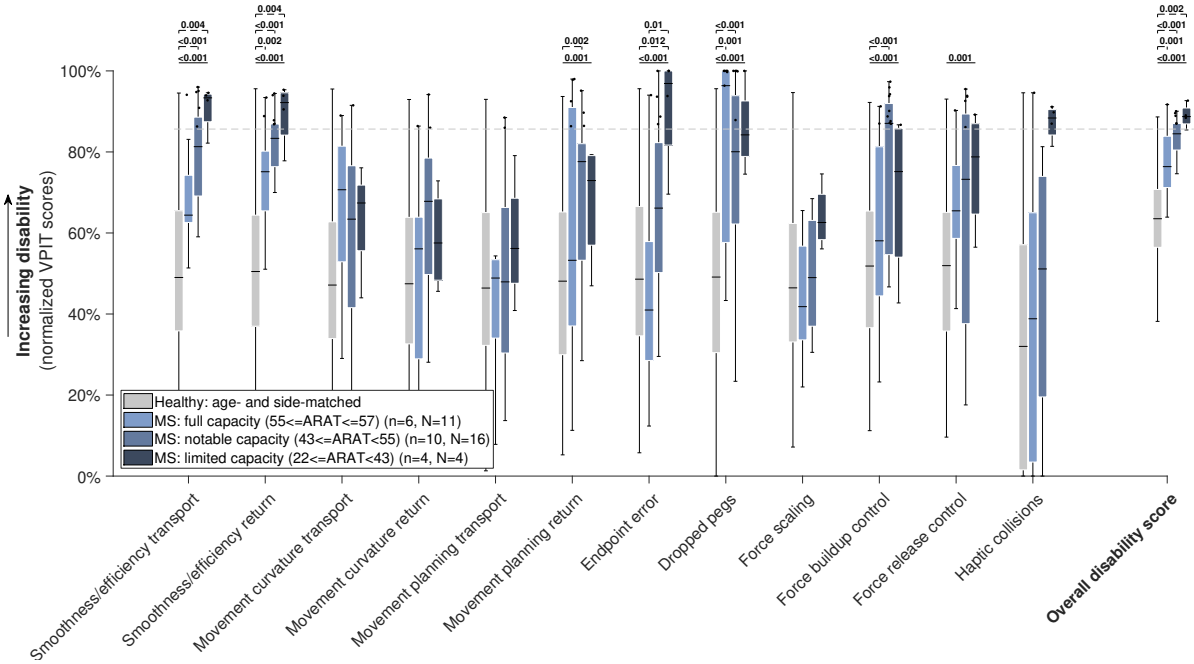


(d) ARSACS patient (age 58 yrs, NHPT time 47.3 s, VPIT time 83.6 s)

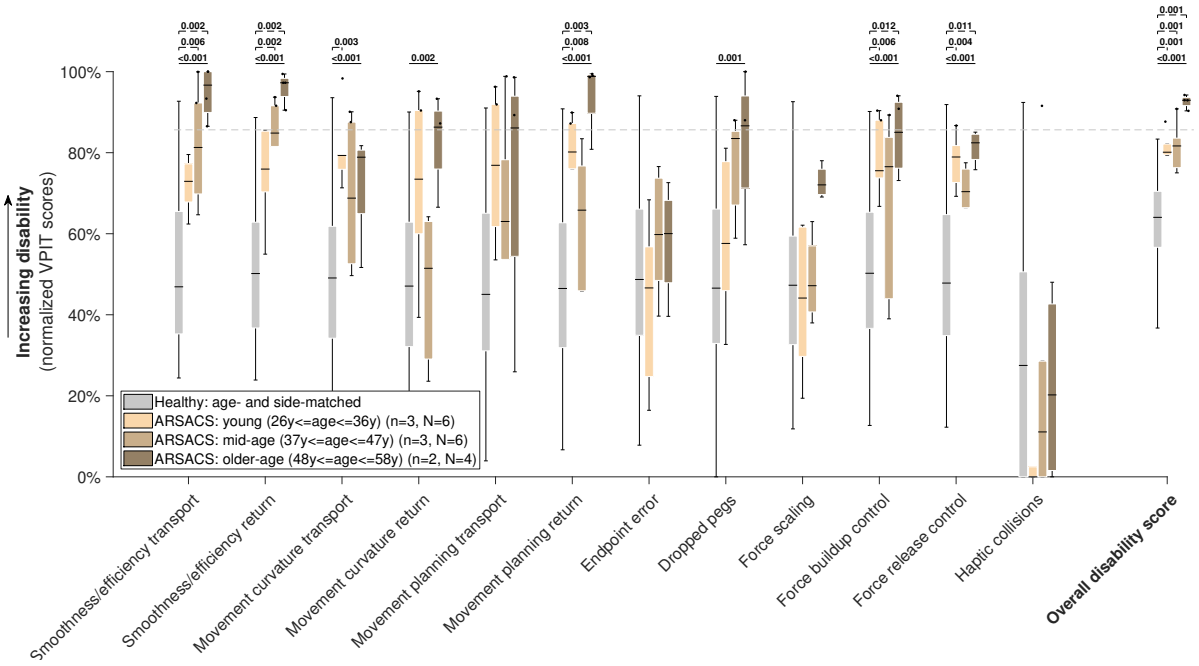
Figure 2: **Representative VPIT trajectories (left) and corresponding sensorimotor profiles (right) of one healthy subject (a) and three patients (b-d).** Increasing size of the sensorimotor components indicates increasing disability scores, which are defined based on underlying probability density functions of age-matched healthy subjects. The mean across five repetitions is visualized for the sensorimotor profile. Abbreviations: MV: Movement. S/E: Smoothness/efficiency. TP: Transport. RT: Return. CV: Curvature. PL: Planning. EE: Endpoint error. DP: Dropped pegs. FS: Force scaling. FBC: Force buildup control. FRC: Force release control. HC: Haptic collisions. Overall: Overall disability.



(a) Stroke population



(b) MS population



(c) ARSACS population

Figure 3: **Discriminant validity of the VPIT sensorimotor profiles.** Three different patient populations were grouped according to their clinical disability level and compared between each subpopulation and to healthy controls. The vertical axis in the sensorimotor profile indicates increasing disability based on the underlying probability density functions of age-matched healthy subjects. In the box plots, the median is visualized through the black horizontal line, the interquartile range (IQR) through the boxes, and the minimum and maximum value within 1.5 IQR of the lower and upper quartile, respectively, through the whiskers. Single data points above the cut-off (horizontal dashed gray line), that is used to discriminate abnormal and healthy behaviour, are represented with black dots. Solid and dashed horizontal black lines above the box plots indicate results of the omnibus and post-hoc statistical tests, respectively Only significant p-value after Bonferroni correction were visualized. The significance level after Bonferroni correction was 0.0038 for the omnibus tests and 0.0125 for the post-hoc tests. The value n refers to the number of subjects in that group and N to the number of data points.