Fakultät für Sport- und Gesundheitswissenschaften

Name der promotionsführenden Einrichtung

Hand kinematics during activities of daily living: The impact of age and neurological disease

Titel der wissenschaftlichen Abhandlung

Philipp Gulde

Vorname und Name

Vollständiger Abdruck der von der

Fakultät für Sport- und Gesundheitswissenschaften

der Technischen Universität München zur Erlangung des akademischen Grades

eines Doktors der Philosophie

genehmigten Dissertation.

Vorsitzende/-r: Prof. Dr. Veit St. Senner

Prüfende/-r der Dissertation:

1. Prof. Dr. Joachim Hermsdörfer

2. Prof. Dr. David Franklin

3. Prof. Dr. Katharina St. Sunnerhagen

Die Dissertation wurde am 15.11.2017 bei der Technischen Universität München eingereicht und durch die

Fakultät für Sport- und Gesundheitswissenschaften am 10.04.2018 angenommen.

Hand kinematics during activities of daily living: The impact of age and neurological disease

Dissertation

Graduate School of the Department of Sport and Health Sciences

Technical University of Munich

Philipp Gulde

25th September, 2017

Abstract

Neurological disease, like dementia or stroke, can impair the ability to perform activities of daily living. Looking at patient samples, they can additionally be heterogeneous in term of their age distribution. Therefore it is necessary to take age into account, when assessing patients' capacities. In this thesis the approach of kinematic analysis of upper-limb end-effector movements is used in order to gain insight into the impact of neurological diseases and age on the performance of activities of daily living and to prove the approach feasible. Further, post-processing techniques were adapted to the complex signal in such activities. Five studies have been conducted. The first study investigated the impact of stroke on the activity of daily living of preparing a cup of tea; the second used the same scenario to examine the kinematic alterations due to aging. The third study assessed the performance of dementia patients in two different activities of daily living and models were computed in order to statistically predict this performance on the basis of kinematics in an abstract sequencing task. Study IV made suggestions towards quantifying movement smoothness in complex tasks, and study five investigated different post-processing methods to handle noise in signals from human upper-limb end-effector movements. Stroke and dementia patients as well as elderly subjects revealed kinematic peculiarities when executing the activities of daily living. Common findings were changed velocities and prolonged inactive phases in the execution of the tasks. A global measure was the trial duration, the time taken to perform the given task. Further, the statistical models were able to predict a big part of the variance in the patient performance of activities of daily living. For the quantification of movement smoothness, the log dimensionless jerk metric was the most appropriate, though none of the metrics was optimal for the complex signals of hand kinematics in activities of daily living. Finally, a local regression algorithm was suggested for the post-processing of noisy signals. The thesis provides a prove of feasibility for the kinematic approach in activities of daily living, delivers further insight into the impact of different neurological diseases on the performance of everyday tasks, and makes methodological suggestions for the optimization of human upper-limb end-effector assessment.

Overview

This thesis is divided in the following main sections:

- The introduction gives an overview on the topics of neurological disease, aging, and activities of daily living.
- The following methods section summarizes the data processing and the out-come measures of the applied approach.
- The third section states the aims and the design of the conducted studies.
- The section ‘Studies’ gives short overviews of the five studies.
- The general discussion of the consolidated studies including a section on limitations and an outlook.
- The affidavit and the list of references.

Content

1 Introduction

Neurological diseases, like stroke or dementia, can impair independent living [1-8]. The daily routine is composed by a variety of single, often independent, activities of daily living. These activities can differ in their degree of complexity, e.g. the opening of a door or the preparation of a meal. Especially deficits in the execution of complex activities can lead to a need of help and care. The reasons for such impairments can be of motor as well as cognitive nature. The motor capacity, that includes gross as well as fine motor skills, can be impaired due to neurological disease, such as dementia of the Alzheimer's type [9-12] or stroke [13-15]. Since activities of daily living are usually in a submaximal range of motor performance, reduced measured capacities in maximum tests, e.g. tapping tasks, do not inevitably lead to impaired motor performance in activities of daily living [16]. Since neurological diseases can also impact cognitive functioning, tasks with lower motor demands can show a reduced performance [17].The relationship between task complexity and performance is moderated by the disease. This means that everyday tasks can be impaired with different degrees of severity by neurological disease [18].

1.1 Stroke

With an incidence rate of 85 per 100.000 person-years (pa) (confidence interval: 76-95/100.000pa; reported for Erlangen, Germany, 1994-1996) and a mortality rate of 19% (1 month case fatality) [19], stroke is one of the leading causes for functional disabilities in western countries [20]. 87% of all strokes are classified as ischemic and 13% hemorrhagic (USA, 1999), with age, sex (female>male), genetics (family history), behaviors (e.g. smoking, inactive lifestyle) and health status (e.g., diabetes mellitus, overweight, high blood pressure) being the main risk factors [20]. In chronic (≥6 months after the stroke) stroke survivors older than 65 years, 26% lost their independence in daily life, 50% suffered from hemiparesis and 46% revealed cognitive deficits, according to Go et al. [20], making stroke related disabilities one the most pressing issues of western societies.

Motor Capacity

Regarding the impact of stroke on the motor capacity, one has to distinguish between the ipsilesional and the contralesional side of the body (in relation to the stroke). The body half contralesional to the side of the brain damage can suffer from paresis, but also in the ipsilesional body half motor impairments can be observed [21-23]. In the clinical setting the motor capacity of the upper-limb and the conceptual abilities of stroke patients are commonly assessment by test batteries like the Birmingham Cognitive Screening (BCoS) [24], the Fugl-Meyer Assessment [25, 26], the Action Research Arm Test (ARAT) [25, 26], the ABILHAND questionnaire [25-27], or the Wolf-Motor-Function Test (WMFT) [28]. Studies that examined the very basic aspects of motor performance looked at tasks like aiming, tapping or prehensile movements. These studies generally revealed reduced frequencies and increased movement times [15, 21-23, 29, 30] as well as intense compensatory movements with the trunk, when testing the contralesional, paretic, side [15, 29-31]. Patients further showed increased lengths of movement trajectories [15], bradykinesia [21-23, 29, 30] and reduced movement smoothness [13, 15]. Still, additional to the tested side of the body (ipsi- or contralesional), it is important on which side of the brain the lesion occurred. For instance, Hermsdörfer [23] only found reduced movement smoothness in patients with right sided brain damage.

Performance of Activities of Daily Living

In stroke patients, not only primary motor impairments, like paresis, can be observed. Patients can show syndromes like apraxia, action disorganization syndrome and neglect, which can cause additional burden, when performing activities of daily living [32]. Deficits in complex, multi-step activities of daily living occur in the form of impaired action planning, commonly showing omissions of necessary actions and false sequencing of such [33-38]. On the other side, patients also show peculiarities in their motor output, i.e. altered movement coordination (velocities, smoothness, directness, trajectories) and timing [39]. Studies examining the impact of stroke on the motor performance of activities of daily living are rare. In these studies the most commonly investigated task is drinking from a glass [25, 26, 40-44]. One of the mentioned studies compared the performance of stroke patients with the performance of age-matched healthy controls [42]. This study examined the impaired, contralesional upper-limb. Similar to the performance in simple tasks, patients revealed increased movement times, a reduced movement speed and smoothness and the aforementioned compensatory trunk movements. The performance when testing the ipsilesional side in an activity of daily living was not measured. The segmentation of a multi-step task into single actions offers the possibility to search for specific burdens, e.g. conceptual deficits or impairments in fine motor control. This was done by Alt Murphy [42] in the drinking task. The analysis of the actions' movement times did not reveal any peculiarity in the stroke patients in comparison to control subjects. Concluding, little is known of the kinematic performance of stroke patients, especially when assessing the ipsilesional upper-limb. However, research utilizing simpler tasks indicates changes in both sides and non-kinematic studies suggest impaired action planning that can have an impact on the kinematic performance.

1.2 Dementia

Dementia reveals an incidence rate of 1070 per 100.000 pa [45], with dementia of the Alzheimer's type being the most prominent one, with approximately 60-70% of all dementia cases [46]. Patients suffering from dementia have an increased risk of having functional disabilities (risk: 49% [47], odds-ratio: 14.0 [48]). Taking into account the high incidence rate and risk of functional disability, dementia is one of the leading socio-economic threats of western societies.

Motor Capacity

The impact of dementia on the motor performance can vary, dependent on the dementia type, the task and the patient's medication. Extrapyramidal symptoms (bradykinesia, rigidity, tremor) can be frequently observed in dementia patients [49], but are often a side-effect of the patients' medication, e.g. haloperidol [50]. Dependent on the task, dementia patients can show comparable (to control subjects) performance in gross motor function, e.g. foot-tapping [11], but reveal declines in fine and complex motor function, already at early stages of dementia or mild cognitive impairment [11, 12]. Further, the type of dementia has an impact on measured motor capacity. Pre-forms like mild cognitive impairment already impair motor performance [9, 11, 12], but especially dementia of the Alzheimer's type or Lewy body dementia [12] reveal high frequencies of extrapyramidal symptoms.

Performance of Activities of Daily Living

In dementia patients, independent living is frequently impaired [1-3, 51]. Reasons for such impairments are beyond the reduced motor capacity. Additional burden is given by the impaired memory function, a loss of focus [52, 53], impaired executive functions [9, 54] and signs of apraxia and action disorganization syndrome [55, 56]. Until now, there has been no examination of the motor performance in activities of daily living, but it has been shown that executive dysfunction and impaired motor capacity are connected with the performance of activities of daily living in dementia and dementia of the Alzheimer's type [57, 58]. However, the capability to execute activities of daily living is assessed on the basis of questionnaires and self-reports of patients [59-61], sight or in best cases using a stopwatch [24, 62-65].

1.3 Aging

Working with patient groups, which suffer from stroke or dementia, the advanced age of the samples has to be taken into consideration. Advanced age alters the performance in simple, as well as, in complex tasks like activities of daily living [18, 66, 67]. Additionally, the age of patient samples can reveal high variance [68]. This especially becomes critical when examining age distributions, in which threshold-like or non-linear reductions in motor performance can be observed [18, 66, 69]. The comparison between patient samples can therefore be restricted due to different age clusters.

Motor Capacity

The impact of age on motor capacity has been examined in a variety of studies, including phase-synchronization tasks [70-75], proprioception [76, 77], movement variability and composition [73, 74, 78-88], bimanual performance [70-72, 74, 75, 89, 90], as well as fine motor control [66] and handwriting [79, 80, 91-94]. The general finding is a decreased motor capacity with advancing age, which shows a clear task complexity x age interaction [82, 88, 90, 95, 96], meaning that the decrement of performance is higher in more complex tasks. Elderly subjects commonly show slowed movements and reaction times, less accurate movements and a reduced movement smoothness [78, 87-90, 95, 97-99], especially in more difficult dual task or choice reaction time task conditions. These obvious limitations in in reaction times have been discussed and the widely acknowledged explanation is a complex age-dependent slowing of in the handling of tasks with a reduced processing speed in the central nervous system [100] and a reduction in cortical lateralization [101] as the basis. However, not every domain of motor performance appears to be influenced by age. For instance, in submaximal conditions, bimanual coordination seems to be not fully affected by age [70-72, 75, 90]. Elderly appear to generate strategies to compensate for their decreased motor capacity. Besides a stronger reliance on visual feedback [102, 103], elderly show changes in their speed-accuracy trade-off in a substantial amount of studies [78, 82, 104, 105] (with an emphasis on accuracy), but it appears to be dependent on the task and its constraints [72, 83, 97, 104]. Another strategy is an increased co-activation of antagonist muscles in order to have a better control of the main movement [85]. Third, a more equal performance and use of both hands have been observed [66, 67], which can be due to a decreased superiority of the dominant hand [66]. This is dependent on the performed task. Poston [87] and Pohl [86] observed comparable or even increased superiority of the dominant hand in aiming-tasks, but indication for a moderation of task difficulty where given.

Performance of Activities of Daily Living

Apart from studies on handwriting, the age-dependent performance in activities of daily living has been only rarely examined. Schaefer [69] observed age-dependent increases in the durations to successfully execute a dressing and a feeding task, limited to an elderly sample with an age-range of 25a (65-89a). Further, Kalisch [66] reported the aforementioned changes in hand use in everyday life (more balanced in advanced age). Bell-McGinty examined the relation of executive functions and functional status in elderly [106]. Using models of multiple linear regression, it was possible to predict 54% of the variance in the functional status, based on The Independent Living Scales questionnaire [107]. However, the capability to perform activities of daily living is, so far, mostly questioned in the presence of disease or post-surgery and not healthy aging.

1.4 Apraxia and Action Disorganization Syndrome

When examining complex, instrumented tasks in neurological disease, it has to be taken into account that patients can suffer from the apraxia and action disorganization syndrome. Until now, it is discussed, if the apraxia and action disorganization syndrome can been seen as one syndrome or two separate impairments [36, 38]. Apraxia describes the inability to perform actions with familiar tools in an “effective and purposeful manner” [36]. Note that this does not apply to all tools or actions. The degree of impairment can vary dependent on the specificity and severity of the neurological disease (i.e. in stroke, the side of the lesion and the affected brain regions or in dementia, the type of dementia and its progression). Action disorganization is the (partial) inability to perform actions that require multiple actions, due to problems putting them in a purposeful and complete order [38, 108]. As mentioned above, it is still discussed, if action disorganization should be seen as one aspect of apraxia. The apraxia and action disorganization syndrome impairs or can even inhibit the performance of activities of daily living. This can be due to the inability to correctly use tools or to sequence necessary actions to achieve the task goal [32, 109]. The prevalence of apraxia in stroke with left sided brain damage is reported between 28% and 51% [110, 111] and in patients with right sided brain damage at approximately 6% [110]. For the prevalence in dementia, apraxia depends on the type of disease. Patients with frontotemporal dementia are reported with 2% [112], while in dementia of the Alzheimer’s type the estimates are between 35% to 98% (dependent on the severity of the dementia) [113, 114]. Even in patients with mild cognitive impairment, signs of apraxia have been reported to be present in 10% of the population [114]. The apraxia and action disorganization syndrome as a frequently observed impairment in stroke as well as in dementia should therefore be considered, when testing clinical populations.

1.5 Assessment of Motor Capacity

The clinical assessment of motor capacity is elaborated, but technological underdeveloped. A substantial amount of tests assessing motor function, applies scores that are based on the trial durations and error frequencies in the execution of tasks [115-122]. Other scorings are made on sight (e.g. Birmingham Cognitive Screening) [24-26, 28] or rely on questionnaires [3, 25-27, 59-61]. Approaches utilizing modern technologies like acceleration sensors or 3-dimensional motion-tracking offer more sensitive and specific analyses of the patient's behavior and first suggestions have already been made [123-126]. With decreasing costs for such technologies, advanced analyses will be stronger embedded in the clinical routine [127, 128]. In the clinical assessment, the influence of cognitive capacity in interaction with the execution of complex motor tasks has so far been only considered to a limited degree. Even in clinical research, the interaction of cognition and complexity and its influence on the motor output has been partially neglected [129]. Reasons could have been the high methodological demands of such analyses [129]. Test, which include a fine motor output (apart from speech) in order to be executed (e.g. trail making tasks or clock drawings) [130-134] are lacking detailed analyses of the end-effector movements in interplay with the cognitive processing of the task.

The kinematic approach offers an objective, specific and sensitive analysis of movements [39, 135-137]. The analysis of movement kinematics does not directly address qualitative parameters like errors. It quantifies movements, applying different aspects, based on the spatio-temporal position of body parts, e.g. end-effectors of upper-limbs. Since cognitive impairments can lead to motor symptoms [138], applying the kinematic approach to activities of daily living does not only offer the possibility to assess motor capacity, but also related cognitive functions.

1.6 Characteristics of Activities of Daily Living

Activities of daily living show a variety of different characteristics and can therefore drastically differ. Such activities can be composed of few up to dozens of single actions, e.g. the opening of a door and the preparation of a meal. The demands on (fine) motor control can be high or low, e.g. tying lacers and swiping a table. They can incorporate only one hand or both, e.g. buttoning a shirt and drinking from a glass. In the case of bimanual activities, they can differ regarding the use of the second hand (loosely based on Woytowicz [139] and Shirota

[140]), i.e. assisting and simultaneously performing a second action, e.g. pouring liquids in cup (assisting), steering a bicycle (same action) and stirring in a pot while adding ingredients (two different actions). The examination of the capability to execute activities of daily living needs a common characteristic that clusters these activities and differentiates them from other tasks. Obhi [129] proposed the object and goal orientation of these activities as a common characteristic. Most activities of daily living involve a least one object that is often manipulated. Additionally, activities of daily living are goal orientated [129]. This means they pursue a goal or effect (Wood [141] speaks of 'products') and have a defined end. Most of the studies on motor capacity lack these aspects. Aiming movements might have a target, but no effect (e.g. the communication of a position), and do not involve objects or object manipulation. Repetitive movements, e.g. oscillating movements with the index finger, do not have a defined end, no goal or effect, and no object or object interaction. Until now, there is a hand full of studies on healthy and patient groups in activities of daily living, which fulfil the criteria proposed by Obhi [8, 14, 25, 42, 135, 136, 142, 143]. However, the chosen activities differ drastically in their degree of complexity and in regard of the amount of possible activities in everyday life, the number of examined tasks is still small and only a few studies assessed more than one activity (most of them in virtual reality) [8, 14, 28, 43]. Further, looking at different activities, there need to be criteria to define their complexity. What makes the preparation of a cup of tea more complex than drinking water from a glass? Wood [141] defined three dimensions of task complexity. The dimension of the component complexity describes the complexity, which arises from the number of necessary actions or steps (Wood speaks of acts) and the associated demand on information processing and storage [144]. Excluded from the number of necessary steps are redundant actions, e.g. the cyclic movements when sawing or hammering. The dimension of coordinative complexity is defined by the relation of actions and products. Parameters are the temporal coordination (parallel, serial, order), the frequency (the number of repetitions), the intensity and the spatial relation (where and how) of actions. The third dimension is the dynamic complexity, which takes into account that certain characteristics as well as the other two dimensions (complexity and coordination) can change in the process of the task. This also applies to an erroneous performance. Applying

these three characteristics on the aforementioned examples of preparing a cup of tea and drinking water from a glass, those activities differ in all three dimensions. The preparation of tea takes more steps and some of them are more demanding on the information storage system, e.g. for how long has the teabag been in the hot water? In both tasks, actions need to be executed in parallel as well as serial, especially when pouring liquids. However, the heated water has higher demands on accuracy, the drinking of water from a glass requires the coordination of head, swallowing and hand movements. The main difference is found in the third dimension, the dynamic complexity. The subcomponents are changing in the process of preparing a cup of tea (in the case of drinking from a glass, only the weight of the glass and its filling level change). A spoon can only be taken to add sugar before stirring the tea and the handling of the water changes with its temperature. Activities of daily can be very complex and it is possible to compare different activities in terms of the three postulated dimensions of complexity. This even accounts for comparisons between activities of daily living and clinical tests.

2 Methods

2.1 Kinematic Analysis

The studies of this thesis are based on spatio-temporal data, obtained by a Qualisys motion capturing system (Qualisys Inc., Gothenburg, Sweden). In the course of the experiments two different settings have been used. The first setting incorporated four Oqus 500+ and one Oqus 510+ cameras, with each camera having a resolution of 4 MP and 120 Hz, and the second incorporating seven Miqus cameras with a resolution of 1 MP and 120 Hz. The system gathers the position of passive, reflective markers with a diameter of 14mm in three dimensional space by triangulation to an accuracy of less than a third of a millimeter. When recording the hand movements executing the activity of daily living, three markers were attached to the anterior third of the dorsum of the hand and the marker with the best coverage was chosen for further analyses. This was due to the incomplete volume coverage of the five camera system and potential covering of the markers by other body parts. When recording the index finger movements in the sequencing task, one marker was attached to the finger nail of the dominant index finger (for the experimental tasks see 3.2). After recording the hand movements, coarse boundaries of the execution (start and end) were set in the track manager software (version 2.10, 2.13 respectively). In a next step, all markers were labelled and in the activity of daily living setting, the marker with the highest coverage for the upper-limb, each upper-limb respectively in bimanual task conditions, was further processed. In rare cases of small gaps in the recordings, polynomial interpolations, offered by the software, were applied. In a next step, the positional data were exported to a MatLab file (*.mat). The data was further processed using MatLab (MathWorks, MA; study I: R2011b, study II & III: R2015a, study IV: R2017a).

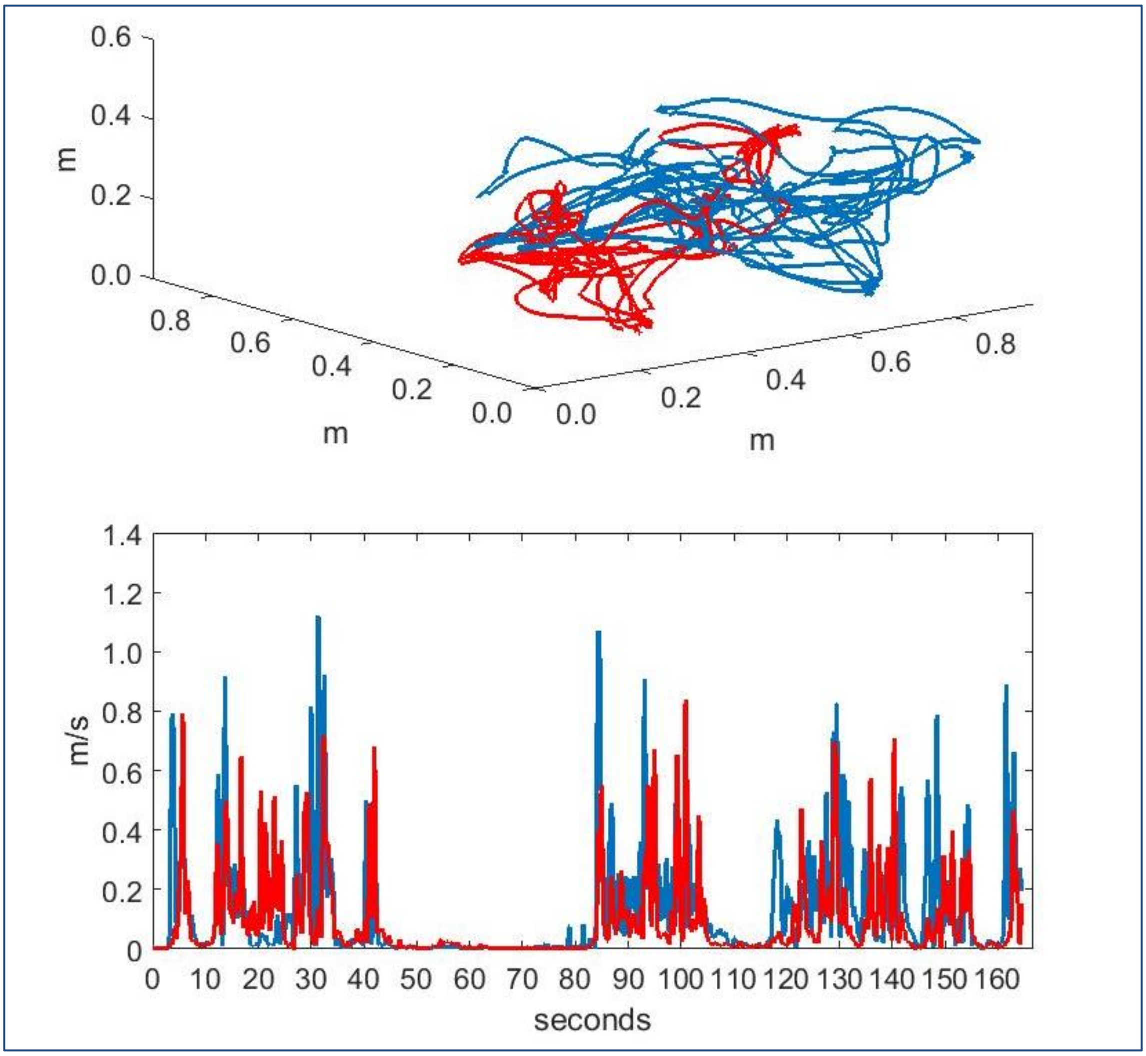

Fig. 1: Examplary display of a movement trajectory in 3D space (upper part) and the corresponding velocity profile (lower part) of an healthy elderly participant performing an activity of daily living (tea making). Red corresponds to the non-dominant left and blue to the dominant right hand. The illustration has been published in [145].

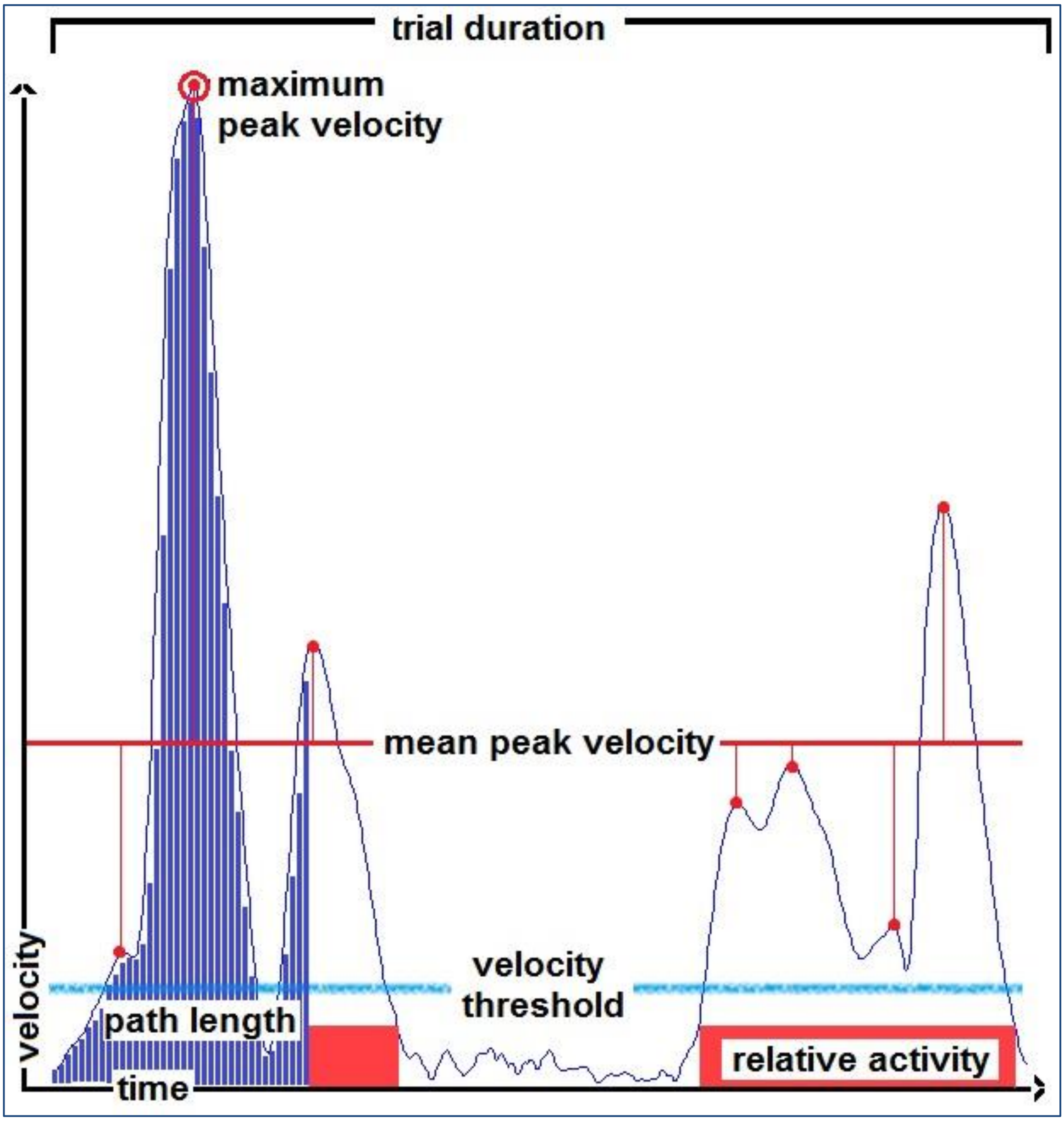

Fig. 2: Illustration of the kinematic parameters trial duration, path length, maximum peak velocity, mean peak velocity and relative activity in a velocity profile of taking a water container, pouring water into a kettle and putting the container back. The illustration has been published in [146].

The positional data were transformed, using triangulation to calculate the distance to the last frame, returning a velocity measure (mm/frame). The velocity was converted to m/s. This velocity profile was smoothed, using local regression filters (‘loess’; study I: 1s span, study II & III: 0.5s span, study IV: 0.1s span). (An evaluation of different smoothing algorithms and filters can be found in 3.7) In a next step, the onset of the first movement and the offset of the last movement were localized and used as start and end points of each trial. The separation of the single actions was based on the same methods, additionally using video footage to define the coarse boundaries of each action. Figure 1 shows examplary movement trajectories and their corresponding velocity profile of a young and an elderly subjects performing an activity of daily living.

The different applied parameters can be put into four different classes. Parameters that are quantifying durations and temporal compositions, parameters quantifying trajectories and spatial compositions, parameters quantifying velocities, and parameters quantifying movement smoothness (loosely based on Reyes-Guzman [39]). Depending on the experiment, different sub-sets of the listed parameters were applied to the velocity profile. Figure 2 illustrates the calculation of some of the common kinematic parameters.

Durations and Temporal Compositions

- **Trial duration [s]:** The trial duration describes the time to execute the whole task. In the activity of daily living of preparing a cup of tea, the passive time when heating the water was excluded. The trial duration is the most commonly used measure. Stroke patients [21, 22, 42, 44, 147, 148], dementia patients [9-11, 149], and elderly [66, 81-83, 87] show increased trial durations in a variety of tasks. The trial duration gives a general estimate of the performance. Since it can be influenced by several factors like motor capacity or processing speed, conclusion on certain functions can only be made, when assessing additional parameters.
- **Movement time [s]:** The movement time quantifies the time to execute a single action, e.g. adding a tea bag to the mug in the activity of daily living of preparing a cup of tea. It is often synonymously used with trial duration.
- **Relative activity:** The relative amount of the trial duration in which the hand, both hands respectively, was/were not moving, defined by a velocity faster than 0.05 m/s. The inactive phases can be considered as accumulated reaction times. Prolonged reaction times have been observed in stroke [137, 147, 150], dementia [9, 151], and aging [95, 97, 100, 152]. Like in reaction times, changes in the relative activity measure can be used to estimate the processing speed.
- **Bimanual cooperation:** The relative amount of the trial duration in which both hands are moving at the same time, defined by a velocity faster than

0.05 m/s. In combination with the path length, the bimanual cooperation can be used to quantify of which kind the bimanual behavior generally was. High values in cooperation and a normal path length can be caused by simultaneously executing two relatively independent actions, while high values in cooperation and in path length can be caused by the non-dominant hand mainly assisting the dominant hand (e.g. for safety reasons) (see 1.6).

- **Frequency [s^{-1}]:** The number of performed movements per second. A reduced frequency in reciprocal aiming tasks and tapping has been reported for stroke [16], dementia [11], and aging [66, 72, 123]. The frequency of performing an action gives valuable information on the (maximum) motor capacity.

Trajectories and Spatial Compositions

- **Path length [m]:** The travelled distance of the corresponding hand. In bimanual condition the path length is the sum of the travelled distances of both hands. Dependent of the tested side of the upper-limb (contra- or ipsilesional), stroke patients can show prolonged path lengths (contralesional limb) [15]. Also in aging, altered lengths of trajectories have been observed [83].
- **Relative vertical path length:** The ratio between path length and distance travelled in the z/vertical-axis. This parameter quantifies the spatial movement composition. In a study on stroke kinematics it has been reported comparable to healthy controls [135].
- **Bimanual quotient:** The ratio of travelled distance of the non-dominant and the dominant hand. Values below 1 correspondent to the dominant hand travelling longer distances. Studies on the bimanual behavior of stroke patients [153-155] and in elderly [66, 70, 72, 73, 75, 90, 156, 157] observed alterations, especially in the frequency of hand use. The applied measures were mostly based on accelerometry in everyday life [66, 153, 156] or different conditions of bimanual performance (see 1.6) in cyclic movements [70, 73, 75].

Velocities

- **Maximum peak velocity [ms^{-1}]:** The highest reached speed in the whole task, or a single action respectively. As a quantification of, depending on the task, maximum motor capacity or general speed of task execution, the maximum peak velocity has been reported decreased in stroke [21, 22, 30, 147] and aging [82, 86, 87], while there have been reports of decreased peak velocities [9] as well as comparable (mean) peak velocities [12] in dementia.
- **Mean peak velocity [ms^{-1}]:** The average of all detected velocity peaks with a threshold of 0.2 of the two highest peaks with a minimum of 0.07 m/s (study I), or with a peak prominence higher than 0.05 m/s (study II & III). The mean peak velocity is an adaptation of the maximum peak velocity to the activity of daily living scenario and is thought to display the general movement speed, especially in submaximal tasks. It rather estimates the processing capacity than the maximum motor capacity, e.g. when subdividing a task or even a movement in several sub-actions the measure will be reduced.

Movement Smoothness and Variability

- **Number of velocity peaks per meter [m^{-1}]:** The quantity of velocity peaks divided by the path length. The velocity peaks have a threshold of 0.2 of the two highest peaks with a minimum of 0.07 m/s (study I), or a minimum peak prominence of 0.05 m/s (study II). The number of velocity peaks per meter is an adapted parameter. Usually the raw number of peaks is used to describe movement smoothness by the number of (sub)movements. In complex tasks with increased degrees of freedom in sequencing the task, the division by the path length is an attempt to normalize the peaks metric. In stroke patients increased number of velocity peaks have been measured [42]. In aging an increased number of movements, defined by velocity peaks, have been measured per second in aiming movements [97]. In dementia a similar measure has been used (velocity direction changes) and revealed decreased movement smoothness in patients in handwriting [12].

- **Relative number of velocity peaks (rNP):** The relative number of velocity peaks is calculated by the ratio of [the difference of the quantity of detected velocity peaks with a threshold of 0.05 m/s and with a minimum peak prominence of 0.05 m/s] and the quantity of detected velocity peaks with a minimum peak prominence of 0.05 m/s.

$$rNP \triangleq \frac{peaks_{minimum} - peaks_{prominence}}{peaks_{prominence}}$$

The relative number of peaks metric is a further adaptation of the number of velocity peaks measure. Additional velocity peaks can result from impairments in inter-muscular coordination or from cognitive processes like changes of movement goals and therefor directions. The relative number of velocity peaks quantifies the amount of additional velocity peaks that have a prominence below 0.05 m/s and should therefore be of motor origin. The measure is, for instance, very sensitive to tremors.

- **Movement harmonicity (MH):** Phase-plotting each forth-and-back (cyclic) movement in a reciprocal task, the relative difference of the ratio of circumference and area of the ellipse-like plot and of the same ratio of an ideal ellipse with the maximum velocity and half the movement amplitude as the radii. For the estimation of the circumference of the ideal ellipse, the approximation by Ramanujan [158] has been used.

$$MH \triangleq \emptyset \frac{\frac{circumference_{measured}}{area_{measured}} - \frac{circumference_{ideal}}{area_{ideal}}}{\frac{circumference_{ideal}}{area_{ideal}}}$$

The movement harmonicity has been used in a related form by Bienkiewicz [14]. It basically quantifies the movement variability in a movement cycle and not between them.

- **Spectral arc length (sarl):** The arc length of the power spectrum of a Fourier transformation of the velocity profile [13].

$$sarl \triangleq -\int_0^{\omega c} \sqrt{\left(\frac{1}{\omega c}\right)^2 + \left(\frac{d\hat{V}(\omega)}{d\omega}\right)^2}\, d\omega, \hat{V}(\omega) \triangleq \frac{V(\omega)}{V(0)}$$

v: velocity profile, [0, ωc]: frequency band, V(ω): Fourier magnitude spectrum

The spectral arc length (sarl) was introduced by Balasubramanian [13] in order to quantify movement smoothness by its frequency components. The arc length of the power spectrum can be influenced by latencies in the onset of overlaying movements, their (sub)movement duration or other factors like for instance tremors or spasticity.

- **Speed metric:** The mean velocity of a velocity profile normalized by its maximum [159]. Since, especially in neurological disease, subjects can reveal unsmooth velocity profiles that consist of a number of single, short movements, the mean velocity is influenced by such breaks. Higher values therefore present higher degrees of movement smoothness.
- **Log dimensionless jerk:** The logarithm naturalis of the sum of the squared acceleration multiplied with the trial duration to the power of three and divided by the squared peak velocity to the power of two [13].

$$log\ dimensionless\ jerk \triangleq -ln\left(\frac{(t_2 - t_1)^3}{v_{peak}^2} \int_{t_1}^{t_2} \left|\frac{d^2 v}{dt^2}\right|^2 dt\right)$$

The basic idea of this metric is that unsmooth movements can alter the relation of acceleration and trial duration. Higher (less negative) values present smoother movements.

2.2 Non-kinematic Analyses

Additionally to the kinematic analyses based on motion capturing, video data were recorded. Based on the video footage, coarse boundaries of single actions were defined. Further, the sequence of actions and committed errors were obtained. Since the tested activities of daily living as well as the sequencing task (for the experimental tasks see 3.2) are composed of several actions, the quantity of actions and their sequence of execution hold information that can not directly be derived from kinematic analyses. So in a first step, the quantity of actions was assessed and compared between the samples in order to check, if a kinematic comparison is legitimate, especially concerning durations and trajectories. Additionally, in the potential presence of apraxia and action disorganization syndrome (see 1.4), the quantity of performed actions could already give details on the severity of the neurological disease. A second analysis used the approach of transition matrices in order to examine the way subjects, especially patients, execute the given task. These matrices also allow a direct comparison of group behaviors by correlational analysis. Each field in such a matrix describes the probability for the transition from one action to another. For a better visual inspection matrices can be displayed as heat maps, after stretching and smoothing (moving average) them. Errors in the performance of activities of daily living were classified based on the work by Hughes [160].This classification contains twelve different error types that have been observed in stroke patients (similar to [161]). Since, the error occurrences of the studied samples of this thesis differed from the original classification by Hughes [160], they were slightly adapted. In the stroke patient sample, three of the error types were used for the analysis:

- **Misestimation errors:** An error by “using grossly too much or too little of some substance” [160], e.g. filling the cup rim full or pouring too little water into the kettle.

- **Execution errors:** “An error in the execution of the task” [160], e.g. knocking something over or dropping a sugar cube.
- **Object substitution errors:** “An intended action carried out with an unintended object” [160], e.g. adding a tea bag with the spoon.

For the elderly sample, frequent peculiarities were collected and then assigned to the different error types by Hughes [160]. The observed error types were:

- **Ingredient omission errors:** Not adding one of the ingredients, e.g. water or milk.
- **Quality errors:** Problems and carelessness in handling the kettle, most frequently not being able to correctly open and close the kettle lid.
- **Mislocation errors:** Not putting the kettle back or the used tea bag to the correct location.
- **Anticipation errors:** Switching on the empty kettle.
- **Misestimation errors:** Filling the mug rim full.

For the dementia sample, the original twelve error type classification was used, and for the abstract sequencing task only sequence errors were possible:

- **Addition errors:** Additional actions.
- **Omission errors:** Omission of actions.
- **Sequence errors:** Wrong order of actions.

2.3 Movement Simulation

The simulation of a upper-limb end-effector velocity profile was based on the work of Flash [162]. The suggested calculation of movements was used to simulate positional data over a trajectory of 0.8 m, including two discrete movements, the first small, the second bigger and composed of two movements with an overlay latency resulting in a double peak in its velocity profile (Fig. 3). The maximum velocity reached was 1.28 m/s. This simulation allows the overlay of noise in order to examine different smoothing algorithms and filters and their settings:

- **Moving average:** The calculation of the mean value over a certain span, e.g. ±10 frames, for each frame of the signal. The signal gets shortened by this method.
- **Local regression:** Similar to the moving average, but instead of the mean, a local regression is calculated. This method is prone to distortions at the start and end of the signal.
- **Butterworth filter:** A frequency filter. Its order describes the damping behavior past the band limit. It can be used as low pass (frequencies above the threshold get filtered), high pass (frequencies below the threshold get filtered) or bandpass (frequencies outside the given range get filtered).

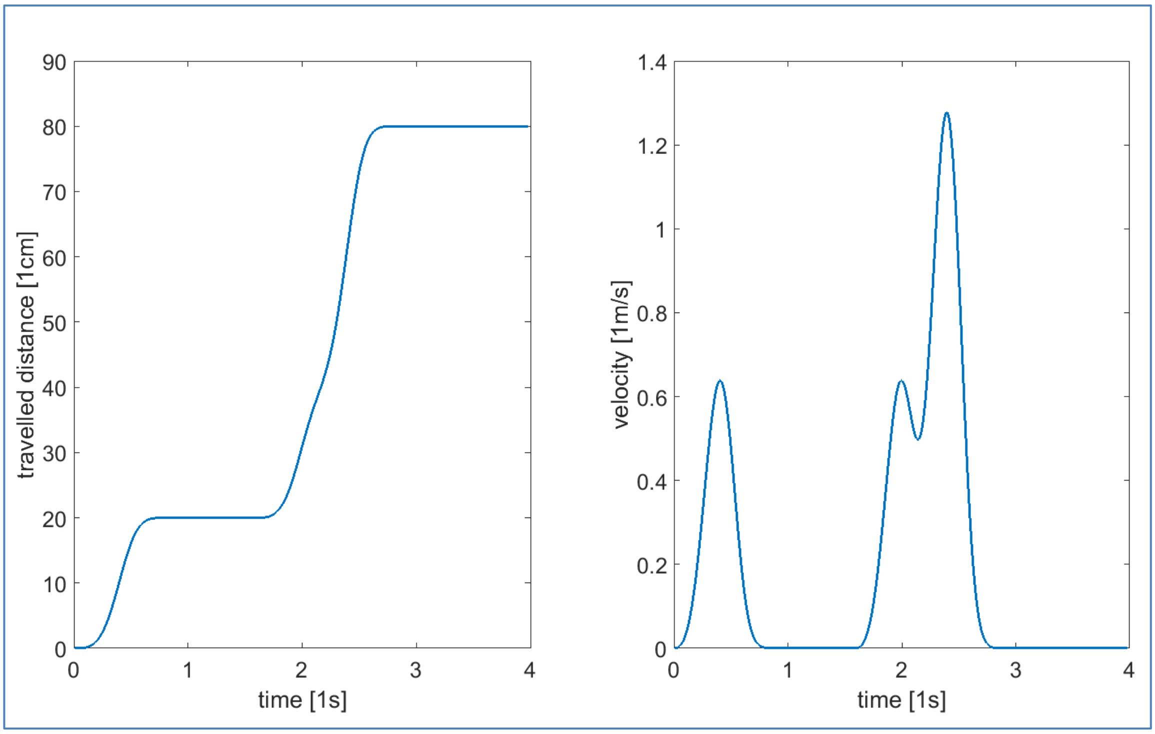

Fig. 3: Simulated trajectory (left) and its corresponding velocity profile (right). The illustration has been published in [163].

2.4 Tasks

In study I, II, III and IV, participants were asked to as naturally as possible perform the activity of daily living of preparing a cup of tea with milk and sugar with no emphasis on speed. Study III included a second activity of daily living, namely the document filing task, and an abstract sequencing task, the reciprocal trail making task.

Tea making task

Participants were asked to prepare a cup of tea with milk and one sugar cube. They were further asked to execute the task as natural as possible and without emphasis on speed. According to the task protocol, a correct execution comprises of eight actions in the following order:

1. Putting water into the kettle
2. Switching the kettle on
3. Adding a tea bag to the mug
4. Pouring the heated water into the mug
5. Removing the tea bag and placing it on the saucer
6. Adding milk
7. Adding sugar
8. Stirring the tea

The working surface with the given object and a distractor item (coffee powder) is displayed in Figure 4.

Fig. 4: Working surface of the tea making task. The illustration has been published in [146].

Document filing task

The seated participants had a working surface with the following objects in front of them: a cardboard file, two sheets of white DIN A4 paper, a hole puncher and a stapler as a distractor item. A laminated picture of the task goal (punched papers in the open cardboard file) was shown to the participants as they were asked to execute the task according to this goal. Participants were instructed to not emphasize on speed of their performance.

Reciprocal trail making task

Participants were asked to put the index finger of their dominant hand on the cross in the center of the task's working surface (Fig. 5). They were further asked to start on signal and touch the given numbers in a rising order with their index finger, returning to the cross after each number. Eight numbers from 03 to 24 in steps of three were given. An exemplary trajectory is displayed in Figure 6.

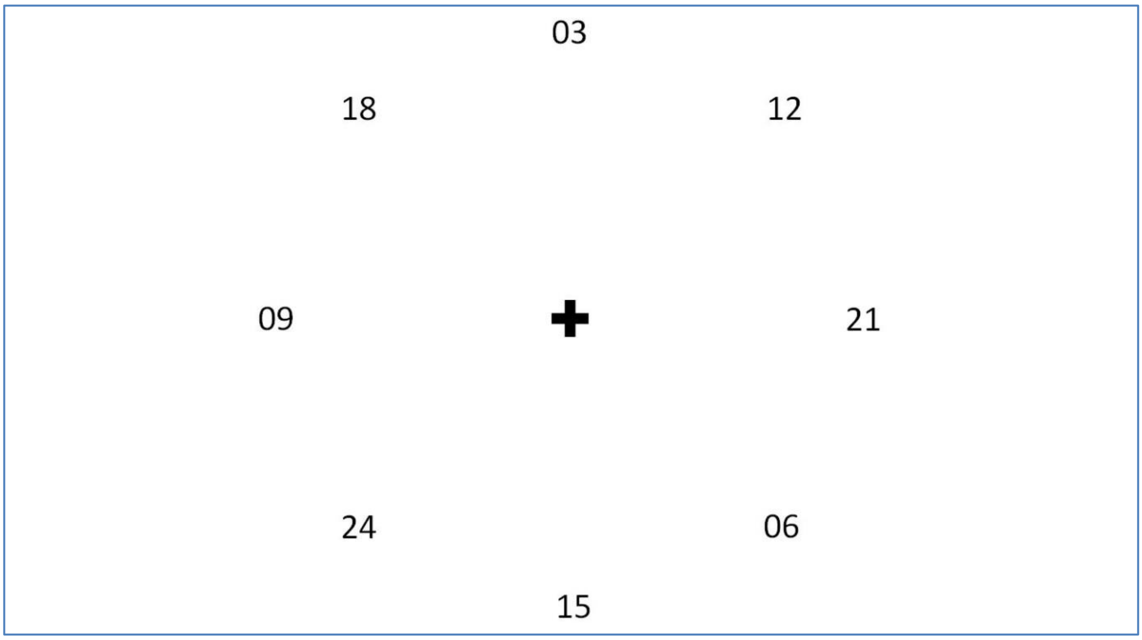

Fig. 5: Working surface of the reciprocal trail making task. This illustration was published in [164].

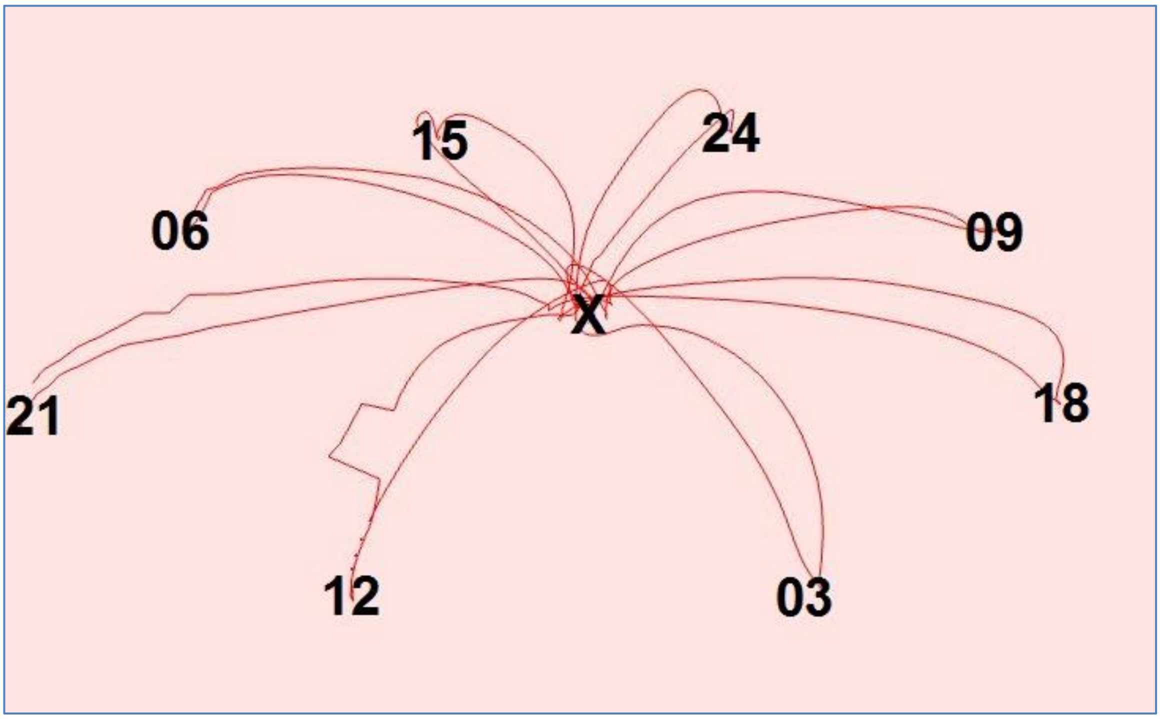

Fig. 6: Trajectory of a healthy young participant performing the reciprocal trail making task. This illustration was published in [164].

3 Studies

3.1 Aims

The main goals of this thesis are the application of the kinematic approach on activities of daily living to investigate the impact of age and different neurological diseases, i.e. stroke and dementia, on multi-step tasks, and second to prove the approach feasible and further develop its methodology. As shown in the introduction, the kinematic approach in activity of daily living scenarios is still at a very early stage, although it has been applied in simple tasks, like aiming, for several decades. Since the structure and complexity of the obtained signal differs from such simple tasks when analyzing activities of daily living, the transfer needs an adaptation of the methodology as well as prove of feasibility. The advantage and justification of such complex and methodologically demanding tasks is their ecological validity. Aiming tasks can give answers to the motor capacity, the processing speed, and in some cases their interaction, but only in the setting of an often maximal demand on (motor) performance. The capability to perform activities of daily living is so far mostly collected by questionnaires. Even in healthy populations, such (self-)estimations are not representing the actual performance, as shown by Kalisch [66] on the topic of handedness and hand use. Based on the gaps in the existing literature, this thesis focusses on the following research questions:

- **Study I:** Is the kinematic approach feasible in detecting and quantifying behavioral peculiarities in stroke patients and how does the disease impact their activity of daily living performance in comparison to healthy, age-matched adults?
- **Study II:** In which way does advanced age impact the kinematic performance in an activity of daily living and of what kind could be underlying mechanisms of such alterations?
- **Study III:** Considering the results of study I and II, is it possible to simulate the cognitive demands of sequencing a multi-step tasks in order to predict activity of daily living performance in dementia patients and what are the differences in comparison to healthy, age-matched adults?

- **Study IV:** Considering study I and II, is there so far a valid and reliable parameter displaying movement smoothness in the complex signals obtained from activities of daily living?
- **Study V:** When obtaining kinematic data, noise in the signal is inevitable. Which post-processing method is the most appropriate in order to reduce noise without losing to much information?

Combining the gained insights of these five studies, this thesis is not only aiming to provide a prove of feasibility of the kinematic approach in activities of daily living, but also new methodological suggestions for post-processing obtained data. It further describes possible burdens and parallels of age and neurological diseases, when handling everyday tasks, and gives a suggestion of how to predict patients' activity of daily living capabilities.

3.2 Study Design

Table 1 offers an overview of the different approaches in the five studies. Study I was a case-control study, in which the kinematic and non-kinematic performance of stroke patients in the activity of daily living of preparing a cup of tea was compared to healthy, age-matched control subjects. Study II was a case-control study, in which the kinematic and non-kinematic performance of health elderly participants in the activity of daily living of preparing a cup of tea was compared to young adults. Study III was a case-control and predictive study, in which the performance of dementia patients in two activities of daily living and an adapted form of the trail making task A were compared to healthy, age-matched control subjects, as well as the estimation of the predictive value of the trail making task on the activity of daily living performance in both groups. Study IV was a methodological study, in which different smoothness parameters were characterized and compared on the basis of velocity profiles of elderly and young participants performing the activity of daily living of preparing a cup of tea. Study V was a simulation, in which different post-processing methods to handle noise were compared and a suggestion of the best fitting, including its settings, was made.

Tab. 1: Overview of the performed experiments, including design, applied tasks, samples, outcome measures and the used statistical methods.

Study	Design	Task(s)	Samples	Outcome measures	Statistical methods
I	Case-control	ADL: tea making	n = 21 7 stroke patients, 3 right sided brain damage, 4 left sided brain damage, 14 healthy, age-matched control subjects	Error scores Number of actions Transition matrices Upper-limb end-effector kinematics	T-test, Repeated measures analysis of variance, Pearson correlation, Cohen's d
II	Case-control	ADL: tea making	n = 26 13 elderly subjects 13 young adults	Error scores Number of actions Upper-limb end-effector kinematics	T-test, Repeated measures analysis of variance, Multivariate analysis of variance, Multiple linear regression, Cohen's d
III	Case-control Predictive	ADL: tea making, data filing, reciprocal aiming task, reciprocal trail making task	n = 29 14 dementia patients 15 healthy, age-matched control subjects	Error scores Upper-limb end-effector kinematics	T-test, Multiple linear regression, Cohen's d
IV	Methodological	ADL: tea making	n = 16 8 elderly subjects 8 young adults	Characteristics of smoothness parameters	T-test, Pearson correlation, Multiple linear regression, Power estimation, Cohen's d
V	Methodological Simulation	-	-	Upper-limb end-effector kinematics	-

Table 2 (next page) provides a list of the manuscripts and their current status of peer-reviewed publication. Please note that two of the papers have been published in 02/2017, one is in a final preparation stage, one is in review, and one is accepted for publication. The author of this thesis is first author in all manuscripts.

Tab. 2: Overview of the studies and their status of publication.

Study	Title	Authors	Journal	Status
I	Effects of Stroke on Ipsilesional End-Effector Kinematics in a Multi-Step Activity of Daily Living	Gulde, P Hughes, CML Hermsdörfer, J	Frontiers in Human Neuroscience	Published (02/2017)
II	Both hands at work: the effect of aging on upper-limb kinematics in a multi-step activity of daily living	Gulde, P Hermsdörfer, J	Experimental Brain Research	Published (02/2017)
III	Step by step: The reciprocal trail making task as a tool to predict ADL performance in dementia	Gulde, P Leippold, K Armstrong, A Kohl, S Grimmer, T Diehl-Schmid, J Hermsdörfer, J	Frontiers in Human Neuroscience	In review
IV	Smoothness metrics in complex movement tasks	Gulde, P Hermsdörfer, J	BioMedical Engineering OnLine	In review
V	A Comparison of Smoothing and Filtering Approaches Using Simulated Kinematic Data of Human Movements	Gulde, P Hermsdörfer, J	Advances in Intelligent Systems and Computing	Published (2018)

3.3 Study I

Effects of Stroke on Ipsilesional End-Effector Kinematics in a Multi-Step Activity of Daily Living

This study was published *in Frontiers in Human Neuroscience* in 02/2017 by Philipp Gulde, Charmayne Hughes and Joachim Hermsdörfer. In this case-control study, the ipsilesional upper-limb end-effector kinematics of stroke patients in the activity of daily living of preparing a cup of tea were compared to healthy, age-matched controls. Patients revealed kinematic peculiarities with no specific burden in the tasks sub-actions. Further, it was hypothesized that the observed alterations are rather based on cognitive impairments than pure motor capacity. In this study, the kinematic approach proved feasible for the assessment of activity of daily living performance.

Contributions:

Philipp Gulde was the primary composer and first author of this manuscript. Charmayne Hughes developed the experimental design, Philipp Gulde and Charmayne Hughes collected the data from the participants. Philipp Gulde and Joachim Hermsdörfer composed the set of parameters. Philipp Gulde performed the post-processing of the gathered positional data and the statistical analyses. All authors contributed to the final manuscript draft.

Abstract:

Stroke frequently impairs activities of daily living (ADL) and deteriorates the function of the contra- as well as the ipsilesional limbs. In order to analyze alterations of higher motor control unaffected by paresis or sensory loss, the kinematics of ipsilesional upper limb movements in patients with stroke has previously been analyzed during prehensile movements and simple tool use actions. By contrast, motion recording of multi-step ADL is rare and patient-control comparisons for movement kinematics are largely lacking. Especially in clinical research, objective quantification of complex externally valid tasks can improve the assessment of neurological impairments. In this preliminary study we employed three-dimensional motion recording and applied kinematic analysis in a multi-step ADL (tea-making). The trials were examined with respect to errors

and sub-action structure, durations, path lengths (PLs), peak velocities, relative activity (RA) and smoothness. In order to check for specific burdens the sub-actions of the task were extracted and compared. To examine the feasibility of the approach, we determined the behavioral and kinematic metrics of the (ipsilesional) unimanual performance of seven chronic stroke patients (64a _ 11a, 3 with right/4 with left brain damage (LBD), 2 with signs of apraxia, variable severity of paresis) and compared the results with data of 14 neurologically healthy age-matched control participants (70a _ 7a). T-tests revealed that while the quantity and structure of sub-actions of the task were similar. The analysis of end-effector kinematics was able to detect clear group differences in the associated parameters. Specifically, trial duration (TD) was increased (Cohen's d = 1.77); the RA (Cohen's d = 1.72) and the parameters of peak velocities (Cohen's d = 1.49/1.97) were decreased in the patient group. Analysis of the task's sub-actions repeated measures analysis of variance (rmANOVA) revealed no impact of the different demands of the sub-actions on the relative performance of the patient group. The analyses revealed kinematic peculiarities in the performance with the ipsilesional hand. These deficits apparently arose from the cognitive demands like sequencing rather than motor constraints. End-effector kinematics proved as a sensitive method to detect and quantify aspects of disturbed multi-step ADL performance after stroke. If standardized, the examination and the analysis are quick and deliver objective data supporting clinical research.

3.4 Study II

Both hands at work: the effect of aging on upper-limb kinematics in a multi-step activity of daily living

This study was published in *Experimental Brain Research* in 02/2017 by Philipp Gulde & Joachim Hermsdörfer. In this case-control study, the bimanual performance of healthy, elderly subjects in the activity of preparing a cup of tea was compared to healthy, young adults. The analyses were based on the upper-limb end-effector kinematics and revealed differences that couldn't be fully derived from the rules known from basic motor tasks. Further, elderly participants revealed different compositions of their trial durations than young adults. It was hypothesized that, similar to the results from study I, the underlying reasons for the kinematic peculiarities are rather based on the task's cognitive than motor demands.

Contributions:

Philipp Gulde was the primary composer and first author of this manuscript. Philipp Gulde collected, post-processed and statistically analyzed the data from the participants. Philipp Gulde and Joachim Hermsdörfer designed the set of parameters. All authors contributed to the final manuscript draft.

Abstract:

The kinematic performance of basic motor tasks shows a clear decrease with advancing age. This study examined if the rules known from such tasks can be generalized to activities of daily living. We examined the end-effector kinematics of 13 young and 13 elderly participants in the multi-step activity of daily living of tea-making. Furthermore, we analyzed bimanual behavior and hand dominance in the task using different conditions of execution. The elderly sample took substantially longer to complete the activity (almost 50%) with longer trajectories compared with the young sample. Models of multiple linear regression revealed that the longer trajectories prolonged the trial duration in both groups, and while movement speed influenced the trial duration of young participants, phases of inactivity negatively affected how long the activity took the elderly subjects. No differences were found regarding bimanual performance or hand dominance. We

assume that in self-paced activities of daily living, the age-dependent differences in the kinematics are more likely to be based on the higher cognitive demands of the task rather than on pure motor capability. Furthermore, it seems that not all of the rules known from basic motor tasks can be generalized to activities of daily living.

3.5 Study III

Step by step: The reciprocal trail making task as a tool to predict ADL performance in dementia

This study is in its final preparation phase. The authors are Philipp Gulde and Joachim Hermsdörfer. In this case-control study the performance of dementia patients in two different activities of daily living and an adapted form of the trail making task A was compared to healthy, age-matched controls. The trial durations for the activities of daily living were strongly prolonged in the patient sample. The patients' performance in the trail making task was impaired in terms of errors and trial durations as well as their kinematic performance. In the patient sample, it was possible to predict the trial durations of the acitivities of daily living by kinematic parameters from the trail making task. The prediction models for the control sample were much weaker in their predictive quality and differed in their composition. It was hypothesized that the used sequencing task held similar cognitive demands as the activities of daily living and can be seen as a preliminary step towards a quick assessment of activity of daily living capabilities.

Contributions:

Philipp Gulde was the primary composer and first author of this manuscript. Philipp Gulde developed the adapted trail making task, post-processed and statistically analyzed the data from the participants. Katharina Leippold was involved in the acquisition of patients and control subjects and performed the qualitative analysis of the activities of daily living. Philipp Gulde, Katharina Leippold and Alan Armstrong collected the lab data from the participants. Alan Armstrong was the primary link to the collaborating clinic Klinikum Rechts der Isar. Sarah Kohl, Timo Grimmer and Janine Diehl-Schmid were responsible for the selection of patients and their clinical assessment. All authors contributed to the final manuscript draft.

Abstract:

Dementia impairs the ability to perform everyday activities. Reduced motor capacity and executive functions as well as loss of memory function and forms of apraxia and action disorganization syndrome can be reasons for such

impairments. In this study, an analysis of the hand trajectories during the sequential movements in an adapted version of the trail making task, the reciprocal trail making task, was used to predict performance in activities of daily living of patients suffering from mild cognitive impairment and dementia. 14 patients with mild cognitive impairment, frontotemporal dementia and dementia of the Alzheimer's type and 15 healthy, age-matched adults were tested in the standardized activities of daily living of tea making and document filing. The characteristics of the kinematic performance in the reciprocal trail making task was assessed and models of multiple linear regression were computed in order to predict the durations of the activities of daily living. Patients showed increased trial durations in the ADL (Cohen's d: tea making 1.58, document filing 1.17). Parameters and explained variability different across patients and control as well as between different activities. The models for the patient sample were stronger and particularly high for the document filing task for which kinematics explained 68% of the variance ($R^2_{adjusted}$: tea making 0.31, document filing 0.68; both tasks combined patients 0.46, controls 0.25). The most relevant factors for the models were the trial duration and a parameter characterizing movement fluency and variability ("movement harmonicity") in the reciprocal trail making task. The models of multiple linear regression suggested that the patients' activity of daily living performance was limited by cognitive demands, namely identifying the varying targets during sequencing, and the healthy controls' performance by their motor capacity. The models further differed strongly in their composition so that generalizations over different activities of daily living are limited.

3.6 Study IV

Smoothness metrics in complex movement tasks

This study is in review in *BioMedical Engineering OnLine* since 06/2017. The authors are Philipp Gulde and Joachim Hermsdörfer. This study examines the behavior of different parameters that are designed to quantify movement smoothness. On the basis of upper-limb end-effector kinematics of healthy, elderly and healthy, young adults in the activity of daily living of preparing a cup of tea, different parameters, selected as agents for four different approaches to describe movement smoothness, were compared. Although, none of the parameters fulfilled all requirements for such complex data, the jerk approach revealed to be the at this point the most appropriate one. Further, suggestions for the different parameters and the prerequisites for their optimal use were made.

Contributions:

Philipp Gulde was the primary composer and first author of this manuscript. Philipp Gulde designed the approach, collected, post-processed and analyzed the data. All authors contributed to the final manuscript draft.

Abstract:

Smoothness is a main characteristic of goal-directed human movements. The suitability of approaches quantifying movement smoothness is dependent on the analyzed signal's structure. Recently, activities of daily living (ADL) received strong interest in research on aging and neurorehabilitation. Such tasks have very complex signal structures and kinematic parameters need to be adapted. In the present is study we examined four different approaches to quantify movement smoothness in ADL. We tested the appropriateness of four different approaches, namely the number of velocity peaks per meter (NoP), the spectral arc length (SpArc), the speed metric (SM) and the log dimensionless jerk (LDJ), by comparing movement signals from eight healthy elderly (67.1a±7.1a) with eight healthy young (26.9a±2.1a) participants performing an activity of daily living (making a cup of tea). All approaches were able to identify group differences in smoothness (Cohen's d NoP=2.53, SpArc=1.95, SM=1.69, LDJ=4.19), three

revealed high to very high sensitivity (z-scores: NoP=1.96±0.55, SpArc=1.60±0.64, SM=3.41±3.03, LDJ=5.28±1.52), three showed low within-group variance (NoP=0.72, SpArc=0.60, SM=0.11, LDJ=0.71), two showed strong correlations between the first and the second half of the task execution (intra-trial correlations R^2s: NoP=0.22 n.s., SpArc=0.33 power<0.80, SM=0.36, LDJ=0.91), and one was independent of other kinematic parameters (SM), while three showed strong models of multiple linear regression (R^2s: NoP=0.61, SpArc=0.48, LDJ=0.70). Based on our results we suggest to use the spectral arc length in tasks with controlled trial durations and movement speeds, to use the number of velocity peaks per meter in tasks with comparable trajectory lengths and number of actions, and the log dimensionless jerk in tasks with controlled trial durations. These are preliminary recommendations based on a relatively small sample size of 2x8.

3.7 Study V

A Comparison of Smoothing and Filtering Approaches Using Simulated Kinematic Data of Human Movements

This study was published in the proceedings of the 11th international Symposium on Computer Science in Sports *Advances in Intelligent Systems and Computing* in 2018. The authors are Philipp Gulde and Joachim Hermsdörfer. In this simulation study, different approaches to eliminate noise in upper-limb end-effector positional signals were compared. It was examined to what degree noise was eliminated and original information was preserved. Based on this analysis a suggestion towards the optimal approach and its settings was made.

Contributions:

Philipp Gulde is the primary composer and first author of this manuscript. Philipp Gulde designed the approach, programmed the simulation and analyzed the data. All authors contributed to the final manuscript draft.

Abstract:

Gathered kinematic data usually requires post-processing in order to handle noise. There a three different approaches frequently used: local regression & moving average algorithms, and Butterworth filters. In order to examine the most appropriate post-processing approach and its optimal settings to human upper limb movements, we examined how far the approaches were able to reproduce a simulated movement signal with overlaid noise. We overlaid a simulated movement signal (movement amplitude 80 cm) with normal distributed noise (standard deviation of 0.5cm). The resulting signal was post-processed with local regression and moving average algorithms as well as Butterworth filters with different settings (spans/orders). The deviation from the original simulated signal in four kinematic parameters (path length, maximum velocity, relative activity, and spectral arc length) was calculated and checked for a minimum. The unprocessed noisy signal showed absolute mean deviations of 54.78% ± 12.16% in the four kinematic parameters. The local regression algorithm revealed the best performance at a span of 420 ms with an absolute mean deviation of 2.00% ± 0.86%. For spans between 280 – 690 ms the local regression algorithm still

revealed deviations below 5%. Based on our results we suggest a local regression algorithm with a span of 420ms for smoothing noisy kinematic data in upper limb performance, e.g., activities of daily living. This suggestion applies to kinematic data of human movements.

4 General Discussion

The general discussion can be seen as an addition to and a summary of the discussions in the manuscripts of the conducted studies. Caused by the emphasis on methodological developments and the clear limitations (see 4.5) of the patient studies, the insights derived from the findings are mostly on the nature of activities of daily living and the methodological developments. Nevertheless, the aims of the thesis were pursued to the maximal degree that was possible by the given resources (e.g. small sample sizes, see 4.5). A short summary of the work performed is followed by a view on the feasibility of the approach, a short discussion on age and neurological disease in activities of daily living, a chapter on the methodological developments, and finally a paragraph on the limitations of the work.

4.1 Summary

In order to examine the feasibility of the kinematic approach, the impact of age and neurological disease on activities of daily living, and to further develop and adapt the kinematic methods to the very complex nature of activities of daily living, five studies have been conducted. The first study investigated the kinematic performance of stroke patients in the activity of preparing a cup of tea. It proved the kinematic approach feasible in such a complex task and further revealed that the constraints appear to be mainly given by the cognitive demands of the task. The second study examined the impact of age on the same task and came to similar conclusions: not every kinematic domain is affected and the impairments indicate the task’s cognitive demands as a key factor. The third study further investigated the assumptions of the first two studies and the performance in activities of daily living in neurological disease (dementia) was statistically predicted by the kinematics in an abstract sequencing task. The findings further support the idea of sequencing being the main limiting factor in the performance of activities of daily living in the assessed samples. The fourth study was of a pure methodological nature and tried to answer the question of how to quantify movement smoothness in activities of daily living and made suggestions for applying different parameters. The fifth study examined different approaches of post-processing noisy data and led to a suggestion for optimal settings.

4.2 Feasibility

The kinematic approach proved feasible in detecting and quantifying the behavioral impact of age and disease. The detection of differences between healthy elderly or young subjects and patients or healthy elderly subjects, respectively, revealed peculiarities in different, but not all, domains of kinematic parameters. The most drastic changes were observed in the trial durations. Due to age, the execution of activities of daily living was already prolonged by approximately 50%. In stroke, trial durations were prolonged by another 50% in comparison to age-matched healthy controls, in dementia even by 100%. Alterations in other kinematic parameters were less consistent. Path length changed due to age (approx. +25%), but not to stroke. The general movement speed was decreased in stroke patients (approx. -25%), but not due to age. The relative activity, the relative amount of time in which the hands were acting, was impacted by stroke (approx. -15%), but not by age. Movement smoothness in activities of daily living was not affected by age or stroke, but this could have been due to an unsuitable parameter (see 3.6). In study V, the elderly sample revealed lower movement smoothness. Further, the bimanual behavior, with respect to age, did not change. So far, it appears that trial duration remains the main criterion in order to estimate task performance in such complex activities. Interestingly, the analysis of single actions in activities of daily living did now reveal any specific burden for the stroke patients, but did for the elderly. A similar approach by Alt Murphy [42] did also not reveal differences in movement times for the single components of the drinking from a glass task. The specific action impact in the elderly sample was interpreted rather as a statistic peculiarity due to high variance in the segment (placing a tea bag in the mug) and in the other segment (stir the tea) as a product of rechecking, if the goal was accurately achieved in the elderly. The segment analysis did probably not reveal a specific motoric or cognitive burden though. Alt Murphy showed that kinematic measures are correlated with a the capacity level after stroke [25] and are responding to clinical improvements [26]. Inversely, in study III (see 3.5), it was possible to statistically predict the trial durations in activities of daily living of dementia patients by kinematic parameters in an abstract sequencing task. There appears to be a strong connection between the performance of activities of daily living and specific clinical tests, although Alt Murphy [25, 26] mainly assessed the motor capacity and study III revealed independence from maximum motor capacity. However, one has to keep in mind the different neurological diseases (stroke (contralesional end-effector) and dementia) of studies. Concluding, the kinematic approach proved feasible, but an analysis of single actions appears not to be necessary, since the impairments appeared to be more global (see Impact of Age & Neurological Disease). Further, the main criterion is the trial duration and therefore coarse, preliminary assessments can already be done using a stopwatch. It has also been shown that activity of daily living performance can be statistically predicted by kinematic parameters of abstract tasks. However, the model for dementia patients was much stronger than the model for healthy controls.

4.3 Impact of Age & Neurological Disease

As aforementioned, age and the examined neurological diseases differ in their impact on kinematics in activities of daily living. A global parameter that is affected by age and both examined diseases is the trial duration. But as revealed by models of multiple linear regression (see 3.4 and 3.5), trial durations are influenced by a variety of different factors that are dependent on the type of disease or age, respectively. The same accounts for clinical scores [26]. The more specific impact of the different conditions is quantified by other parameters. These do reveal most different impacts of age and disease. However, typical patient samples suffering from stroke or dementia are of advanced age, so such patients are impacted by both, age and disease. Since it has been reported that there are also differences in the elderly [66, 95], it can be stated that age impacts the kinematic performance in activities of daily living, but same as for neurological diseases with different etiologies or severities, it is hard to generate rules other than very broad statements like ‘slowed movements’ or ‘reduced accuracy’. Still, the individual performance can be accurately assessed and further estimates can be made by statistical models. Nevertheless, the conducted studies lead to some assumptions:

- Declines in the performance of activities of daily living due to age or disease are rather caused by cognitive than motor demands.
- Not all rules from simpler tasks can be applied to activities of daily living.
- Activities of daily living are very complex and of submaximal nature in terms of their demands on motor function.
- Activities of daily living are a group of actions with common features, but still show a huge variety of demands.
- There is a lack in the quantity of different examined activities of daily living.

It is expected that in future at least some of the given statements will be further studied, but due to the very heterogeneous nature of the subjects (neurological disease, age, and activities of daily living) progress will be limited and the methodology has to be further adapted.

4.4 Methodological Developments

The methodological developments of the conducted studies can be put into three different classes: 1) post-processing, 2) kinematic parameters, and 3) statistical methods.

Post-processing

The applied smoothing/filtering approaches for the post-processing of kinematic data in activities of daily living are not standardized. Dependent on the original field of study, researchers apply different methods; engineers and biomechanics commonly use Butterworth filters, others are using algorithms like moving averages or local regressions. Additionally, the settings of those tools are not standardized. The basic idea of those post-processing approaches is to handle noise without losing information. This was investigated in study V (see 3.7). At least in this very specific simulated movement with the added noise, the local regression filter with a span of 420ms (given a sampling rate of 100 Hz in the original signal) performed best and was able to reduce the loss of information in typical kinematic parameters (path length, movement smoothness, speed and so on) from approximately 55% to 2%. Spans of 280ms to 690ms still resulted in losses of below 5%. In post-hoc consideration of the applied filters in studies I-III, the settings of the applied local regression filters were not optimal in the stroke study with a span of 1000ms (see 3.7) This could have led to information losses of over 10%. In hindsight, study V should have been conducted at first in order to get optimal setting for the applied smoothing algorithm, especially in the patient study (study I).

Kinematic Parameters

Trial duration proved to be the most global parameter. It can be easily assessed and provides a good estimate of performance, but at a high variance. It has been used to quantify the performance of activities of daily living in study III (see 3.5). Schaefer [69] even limited the assessment of performance to the trial duration. The models of multiple linear regression and correlational analyses in studies I, II, and III (see 3.3, 3.4, and 3.5) nevertheless underline that there are different factors impacting the trial duration and analyses should apply more parameters. The method of examining the composition of the trial duration by phases of activity and inactivity is basically not new, but it was rather used to describe movement smoothness in simpler tasks [159]. In stroke patients the relative activity was decreased and in elderly subjects it significantly contributed to the variance in trial duration. The approach of interpreting the passive phases as accumulated reaction times offers the kinematic analysis of activities of daily living a direct access to changes or deficits in processing speed. The path length and related parameters, e.g. the bimanual quotient, also revealed high variance. Although it has been shown for the path length, same as for ranges of motion in joints or amplitudes in cyclic tasks, that the path length can help to quantify certain aspects of neurological disease [21, 42, 138], the length of the trajectories only showed differences in dependence on age and also its composition (relative vertical path length) was unobtrusive. However, path length contributes to a large amount to the variance in trial durations and should therefore be assessed, at least in order to control for it. The commonly used parameter of maximum peak velocity was adapted to better fit signals including multiple actions. The resulting mean peak velocity proved more sensitive (see 3.3) than the maximum peak velocity. The parameter revealed differences in stroke and dementia patients and in manual conditions. Its advantage is that it accounts every action in order to estimate a general and not a maximum working speed, which is more appropriate for the assessment of upper-limb end-effector behavior in activities of daily living. Study II inter alia examined the impact of different hand conditions on the performance. This impact is important when assessing stroke patients in unimanual conditions and comparing them with healthy adults, since the conditions revealed strong differences in several parameters (see 3.4**Fehler! Verweisquelle konnte nicht gefunden werden.** or [69]). The used parameters to quantify bimanual performance were the bimanual quotient and the bimanual cooperation. The bimanual quotient is the relation of travelled path length of dominant and non-dominant hand and the bimanual cooperation is the relative amount of time of both hands being active. There was no difference in the bimanual behavior of young and old participants. This could be due to unchanged movement patterns, although literature indicates such changes, at least in everyday life [66]. However, both parameters revealed relatively high variance and this indicates that an optimization of the underlying calculations should be performed, since patient groups were reported to have altered hand use [153, 156, 165]. Measures of movement smoothness, as examined in study IV (see 3.6), proved to be not best fitting to the characteristics of activities of daily living. Nevertheless, suggestions were made on the basis of movement data of young and elderly adults. The underlying approach differed from the commonly used simulation methods [13, 159] and examined a variety of characteristics of the outcome measures. All used parameters were able to detect group differences, but they strongly differed in terms of within-group variance, intra-trial correlation and their dependence from typical kinematic parameters. Although none of the examined smoothness parameters proved to be fully suited, the log dimensionless jerk measure performed best to quantify movement smoothness in the examined activity of daily living. In hindsight, the used peaks metric in studies I and II was not appropriate for the elderly/young comparison since one the suggested prerequisites was not given (comparable path lengths). However, the prerequisites for the spectral arc length or log dimensionless jerk were given neither.

Statistical Methods

Alt Murphy [42] performed an analysis of the single actions of the drinking from a glass task based on the trial durations. In study I and II, the approach was broadened to a variety of kinematic parameters. Similar to Alt Murphy [42], stroke patients did not reveal specific burdens. The elderly sample did, but the statistical outcome was not very comprehensive. If such analyses are feasible in the kinematic analyses of activities of daily living is questionable, since the segmentation of a task comes with a high workload. The application of transition matrices in order to examine the sequencing of the task was so far without significant results (see 3.3 and 3.4). This might have been caused by the self-correction of participants. There have been signs for higher cognitive loads of sequencing on elderly and patients in the kinematic analyses. Another reason could have been that correlational analyses of such matrices where inappropriate. Other possibilities would have been simulations or cluster analyses. The use of models of multiple linear regressions, as for instance already applied by Alt Murphy [25], proved to be a powerful statistical tool to examine kinematic data. It was possible to identify different strategies in performing the tea making task in elderly and young (see 3.4) and strong predictions were made for dementia patients (see 3.5). Since patient groups are commonly heterogeneous and comprise a variety of interfering factors, a future direction could be the application of mixed linear models to examine their kinematic behavior.

4.5 Limitations

Clear limitations are given due to the sample sizes of the studies. Especially study I with seven patients, four with left brain damage and three with right brain damage, has very limited power. Further, as aforementioned (see 4.3), limitations are given by the heterogeneity of samples of patients with neurological diseases, by the appliance of not fully appropriate post-processing of the signal, and by the unfulfilled prerequisites of the applied smoothness parameter. Another limitation is the small spectrum of examined activities of daily living. However, especially the methodological conclusion drawn from the conducted studies make significant suggestions to the field of kinematic analyses of upper-limb end-effectors in activities of daily living.

4.6 Outlook

This thesis provides insights into neurological diseases, i.e. stroke and dementia, and aging, activities of daily living, the kinematic approach, and applicable methodologies. Neurological disease as well as age drastically impacts the performance of activities of daily living. The kinematic analysis of such performance is an appropriate tool and suggestions are made of how to best post-process the spatio-temporal positions of upper-limb end-effectors. The adaptation and development of parameters is still at a relative early stage and future studies will provide more powerful tools that enable even more sensitive investigations. The significance of kinematic analyses is expected to increase in the near future due to the falling costs of motion capturing devices and the fast developing virtual and augmented reality sector.

5 Statutory Declaration / Affidavit

I hereby confirm that the dissertation ‘Hand kinematics during activities of daily living: The impact of age and neurological disease’ is the result of my own work and that I have only used sources or materials listed and specified in the dissertation.

Munich 25th September, 2017

Philipp Gulde

6 Reference List

1. Reisberg, B., et al., *The Alzheimer's Disease Activities of Daily Living International Scale (ADL-IS).* International Psychogeriatrics, 2001. **13**(2).
2. Pedrosa, H., et al., *Functional evaluation distinguishes MCI patients from healthy elderly people - The ADCS/MCI/ADL scale.* The journal of nutrition, health & aging, 2010. **14**(8): p. 703-709.
3. Perneczky, R., et al., *Impairment of activities of daily living requiring memory or complex reasoning as part of the MCI syndrome.* Geriatric Psychiatry, 2006. **21**(2): p. 158-162.
4. Foundas, A., et al., *Ecological implications of limb apraxia: evidence from mealtime behavior.* Journal of the International Neuropsychological Society, 1995. **1**: p. 62-66.
5. Forde, E. and G. Humphreys, *The role of semantic knowledge and working memory in everyday tasks.* Brain and Cognition, 2000. **44**: p. 214-252.
6. Hartmann, K., et al., *It takes the whole brain to make a cup of coffee: the neuropsychology of naturalistic actions involving technical devices.* Neuropsychologia, 2005. **43**: p. 625-637.
7. Schwartz, M., *The cognitive neuropsychology of everyday action and planning.* Cognitive Neuropsychology, 2006. **23**: p. 202-221.
8. Wisneski, K. and M. Johnson, *Quantifying kinematics of purposeful movements to real, imagined, or absent functional objects: implications for modelling trajectories for robot-assisted ADL tasks.* Journal of NeuroEngineering and Rehabilitation, 2007. **4**(7).
9. Camarda, R., et al., *Movements executiuon in amnestic mild cognitive impairement and Alzheimer's disease.* Behavioral Neurology, 2007. **18**: p. 135-142.
10. Ghilardi, M.-F., et al., *Impaired movement control in Alzheimer's disease.* Neuroscience Letters, 1999. **260**: p. 45-48.
11. Kluger, A., et al., *Patterns of Motor Impairment in Normal Aging, Mild Cognitive Decline, and Early Alzheimer's Disease.* Journal of Gerontology: Psychological Sciences, 1997. **52B**(1): p. 28-39.
12. Schröter, A., et al., *Kinematic Analysis of Handwriting Movements in Patients with Alzheimer's Disease, Mild Cognitive Impairment, Depression and Healthy Subjects.* Dementia and Geriatric Cognitive Disorders, 2002. **15**: p. 132-142.
13. Balasubramanian, S., A. Melendez-Calderon, and E. Burdet, *A Robust and Sensitive Metric for Quantifying Movement Smoothness.*

IEEE Transactions on Biomedical Engineering, 2012. **59**(8): p. 2126-2136.

14. Bieńkiewicz, M., et al., *Harmonicity of the movement as a measure of apraxic behavior in stroke survivors.* Biosignals, 2014: p. 295-300.
15. Cirstea, M. and M. Levin, *Compensatory strategies for reaching in stroke.* Brain, 2000. **123**: p. 940-953.
16. Ietswaart, M., D. Carey, and S. Della Sala, *Tapping, grasping and aiming in ideomotor apraxia.* Neuropsychologia, 2006. **44**: p. 1175-1184.
17. Goldman, W., et al., *Motor dysfunction in mildly demented AD individuals without extrapyramidal signs.* Neurology, 1999. **53**(5): p. 956.
18. Scherder, E., W. Dekker, and L. Eggermont, *Higher-Level Hand Motor Function in Aging and (Preclinical) Dementia: Its Relationship with (Instrumental) Activities of Daily Life - A Mini-Review.* Gerontology, 2008. **54**: p. 333-341.
19. Feigin, V., et al., *Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review.* The Lancet. Neurology., 2009. **8**(4): p. 355-369.
20. Go, A., et al., *Heart Disease and Stroke Statistics – 2013 Update*. 2013, American Heart Association: Dallas, TX.
21. Laimgruber, K., G. Goldenberg, and J. Hermsdörfer, *Manual and hemispheric asymmetries in the execution of actual and pantomimed prehension.* Neuropsychologia, 2005. **43**: p. 682-692.
22. Tretriluxana, J., et al., *Hemisphere Specific Impairments in Reach-to-Grasp Control After Stroke: Effects of Object Size.* Neruorehabilitation and Neural Repair, 2009. **23**: p. 679-691.
23. Hermsdörfer, J., et al., *Prehension with the ipsilesional hand after unilateral brain damage.* Cortex, 1999. **35**: p. 139-161.
24. Bickerton, W., et al., *Systematic assessment of apraxia and functional pedictions from the Birmingham Cognitive Screen.* Journal of neurology, neurosurgery & psychatry with practical neurology, 2012. **85**(5): p. 512-552.
25. Alt Murphy, M., C. Willén, and K. Sunnerhagen, *Movement Kinematics During a Drinking Task Are Associated With the Activity Capacity Level After Stroke.* Neurorehabilitation and Neural Repair, 2012. **26**(9): p. 1106-1115.
26. Alt Murphy, M., C. Willén, and K. Sunnerhagen, *Responsiveness of Upper Extremity Kinematic Measures and Clinical Improvement During the First Three Months After Stroke.* Neurorehabilitation and Neural Repair, 2013. **27**(9): p. 844-853.

27. Penta, M., et al., *The ABILHAND questionnaire as a measure of manual ability in chronic stroke patients: Rasch-based validation and relationship to upper.limb impairment.* Stroke, 2001. **32**(7): p. 1627-1634.
28. Adams, R., et al., *Assessing Upper Extremity Motor Function in Practice of Virtual Acitivities of Daily Living.* IEEE Transactions on Neural Systems and Rehabilitation Engineering, 2015. **23**(2): p. 287-296.
29. Michaelsen, S., E. Magdalon, and M. Levin, *Grip aperture Scaling to Object Size in Chronic Stroke.* Motor Control, 2009. **13**: p. 197-217.
30. Michaelsen, S., et al., *Compensation for distal impairments of grapsing in adults with hemiparesis.* Experimental Brain Research, 2004. **157**: p. 162-173.
31. Roby-Brami, A., et al., *Reaching and grasping strategies in hemiparetic patients.* Motor Control, 1997. **1**: p. 72-91.
32. Bieńkiewicz, M., et al., *The complexity of the relationship between neuropsychological deficits and impairment in everyday tasks after stroke.* Brain and Behavior, 2015. **5**(10).
33. Buxbaum, L., *Ideational apraxia and naturalistic action.* Cognitive Neuropsychology, 1998. **15**: p. 617-643.
34. Schwartz, M., et al., *Naturalistic action production following right hemisphere stroke.* Neuropsychologia, 1999. **37**: p. 51-66.
35. Bickerton, W., G. Humphreys, and M. Riddoch, *The case of the unfamiliar implement: schema-based over-riding of semantic knowledge from objects in everyday action.* Journal of the International Neuropsychological Society, 2007. **13**: p. 1035-1046.
36. Bieńkiewicz, M., et al., *The tool in the brain: apraxia in ADL. Behavioral and neurological correlates of apraxia in daily living.* Frontiers in Psychology, 2014. **5**(353).
37. Sunderland, A., C. Walker, and M. Walker, *Action errors and dressing disability after stroke: an ecological approach to neuropsychological assessment and intervention.* Neuropsycholigcal Rehabilition, 2006. **16**: p. 666-683.
38. Humphreys, G. and E. Forde, *Disordered action schema and action disorganisation syndrome.* Cognitive Neuropsychology, 1998. **15**: p. 771-811.
39. de los Reyes-Guzmán, A., et al., *Quantitative assessment based on kinematic measures of functional impairments during upper extremity movements: A review.* Clinical Biomechanics, 2014. **29**(7): p. 7119-727.

40. Weiss, P., et al., *Is the organization of goal-directed action modality specific? A common temporal structure.* Neuropsychologia, 2000. **38**: p. 1136-1147.
41. Alt Murphy, M., et al., *Three-dimensional kinematic motion analysis of a daily activity drinking from a glass: a pilot study.* Journal of NeuroEngineering and Rehabilitation, 2006. **3**(18).
42. Alt Murphy, M., C. Willén, and K. Sunnerhagen, *Kinematic Variables Quantifying Upper-Extremity Performance After Stroke During Reaching and Drinking From a Glass.* Neurorehabilitation and Neural Repair, 2011. **25**(1): p. 71-80.
43. Thies, S., et al., *Movement variability in stroke patients and controls performing two upper limb functional tasks: a new assessment methodology.* Journal of NeuroEngineering and Rehabilitation, 2009. **6**(2).
44. Kim, K., et al., *Kinematic analysis of upper extremity movement during drinking in hemiplegic subjects.* Clinical Biomechanics, 2014. **29**: p. 248-256.
45. Ott, A., et al., *Incidence and Risk of Dementia: The Rotterdam study.* American Journal of Epidemiology, 1998. **417**(6): p. 574-580.
46. Fratiglioni, L., et al., *Incidence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. Neurologic disease in the Elderly Research Group.* Neurology, 2000. **54**(11): p. 10-15.
47. Agüero-Torres, H., et al., *Dementia is the major cause of functional dependence in the elderly: 3-year follow-up data from a population-based study.* American Journal of Public Health, 2011. **88**(10): p. 1452-1456.
48. Sauvaget, C., et al., *Dementia as aPredictor of Functional Disability: A Four-Year Follow-Up Study.* Gerontology, 2002. **48**: p. 226-233.
49. Tyrrell, P., G. Sawle, and V. Ibanez, *Clinical and Positron Emission Tomographic Studies in the 'Extrapyramidal Syndrome' of Dementia of the ALzheimer Type.* Archives of Neurology, 1990. **47**(12): p. 1318-1323.
50. De Deyn, P., et al., *A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia.* Neurology, 1999. **53**(5): p. 946.
51. Bettcher, B., et al., *Improving Everyday Error Detection, One Picture at a Time: A Performance-Based Study of Everyday Task Training.* Neuropsychology, 2011.
52. Navia, B., B. Jordan, and R. Price, *The AUDS dementia complex: I. Clinical features.* Anals of Neurology, 1986. **19**(6): p. 517-524.

53. Neary, D., et al., *Clinical and neuropathological criteria for frontotemporal dementia.* Journal of neurology, neurosurgery & psychiatry with practical neurology, 1994. **57**(4): p. 416-418.
54. Ott, B., S. Ellias, and M. Lannon, *Quantitative assessment of movement in Alzheimer's disease.* Journal of Geriatric Psychiatry and Neurology, 1995. **8**(1): p. 71-75.
55. Ochipa, C., L. Rothi, and K. Heilman, *Conceptual Apraxia in Alzheimer's Disease.* Brain, 1992. **115**(4): p. 1061-1071.
56. Rapcsak, S., S. Croswell, and A. Rubens, *Apraxia in Alzheimer's disease.* Neurology, 1989. **39**(5): p. 664.
57. Boyle, P., et al., *Cognitive and motor impairments predict functional declines in patients with vascular dementia.* International Journal of Geriatric Psychiatry, 2002. **17**(2): p. 164-169.
58. Boyle, P., et al., *Executive Dysfunction and Apathy Predict Functional Impairment in Alzheimer Disease.* The American Journal of Geriatric Psychiatry, 2001. **11**(2): p. 214-221.
59. Douglas, G., et al., *An Inventory to Assess Activities of Daily Living for Clinical Trials in Alzheimer's Disease.* Alzheimer Disease& Associated Disorders, 1997. **11**(2): p. 33-39.
60. Pincus, T., et al., *Assessment of patient satisfaction in activities of daily living using a modified stanford health assessment questionnaire.* Athritis & Rheumatology, 1983. **26**(11): p. 1346-1353.
61. Bucks, R., et al., *Assessment of Activities of Daily Living in Dementia: Development of the Bristol Activities of Daily Living Scale.* Age and Ageing, 1996. **25**: p. 113-120.
62. Ehrensperger, M., et al., *Early detection of Alzheimer's disease with a total score of the German CERAD.* Journal of the International Neuropsychological Society, 2010. **16**: p. 910-920.
63. Carr, D., et al., *Predicting Road Test Performance in Drivers with Dementia.* Journal of the American Geriatric Society, 2011. **59**(11): p. 2112-2117.
64. Goldenberg, G., *Defective imitation of gestures in patients with damage in the left or right hemisphere.* Journal of Neurology, Neurosurgery and Psychiatry, 1996. **61**: p. 176-180.
65. Baumard, J., et al., *Tool use disorders in neurodegenerative diseases: Roles of semantic memory and technical reasoning.* Cortex, 2016. **82**: p. 119-132.
66. Kalisch, T., et al., *Age-Related Attenuation of Dominant Hand Superiority.* PLoS One, 2006. **1**(1).
67. Przybyla, A., et al., *Motor Asymetry Reduction in Older Adults.* Neuroscience Letters, 2011. **489**(2): p. 99-104.

68. Seshadri, S., et al., *The Lifetime Risk of Stroke.* Stroke, 2006. **37**: p. 345-350.
69. Schaefer, S., *Preserved motor asymmetry in late adulthood: is measuring chronological age enough?* Neuroscience, 2015. **294**: p. 51-59.
70. Bangert, A., et al., *Bimanual Coordiantion and Aging: Neurobehavioral Implications.* Neuropsychologia, 2010. **48**(4): p. 1165-1170.
71. Goble, D., et al., *The Neural Control of Bimanual Movements in the Elderly: Brain Regions Exhibiting Age-Related Increases in Activity, Frequency-Induced Neural Modulation, and Task Specific Compensatory Recruitment.* Human Brain Mapping, 2010. **31**(8): p. 1281-1295.
72. Lee, T., L. Wishart, and J. Murdoch, *Aging, Attention, and Bimanual Coordination.* Canadian Journal of Aging 2002. **21**(4): p. 549-557.
73. Serrien, D., S. Swinnen, and G. Stelmach, *Age-Related Deterioration of Coordinated Interlimb Behavior.* Journal of Gerontology, 2000. **55B**(5): p. 295-303.
74. Temprado, J.-J., et al., *A Dynamic Systems Approach to the Effects of Aging on Bimanual Coordination.* Gerontology, 2009. **56**(3): p. 335-344.
75. Wishart, L., et al., *Effects of Aging on Automatic and Effortful Processes in Bimanual Coordination.* Journal of Gerontology, 2000. **55B**(2): p. 85-94.
76. Adamo, D., B. Martin, and S. Brown, *Age-Related Differences in upper Limb proprioceptive Acuity.* Perceptual and Motor Skills, 2007. **104**: p. 1297-1309.
77. Kaplan, F., et al., *Age-Related Changes in Proprioception and Sensation of Joint Position.* Acta Orthopaedica Scandinavica, 1985. **56**(1): p. 72-74.
78. Christou, E., M. Shinohara, and R. Enoka, *Fluctuations in acceleration during voluntary contractions lead to greater impairment of movement acuracy in old adults.* Journal of Applied Physiology, 2003. **95**: p. 373-384.
79. Contreras-Vidal, J., H. Teulings, and G. Stelmach, *Elderly subjects are impaired in spatial coordination in fine motor control.* Acta Psychologica, 1998. **100**: p. 25-35.
80. Teulings, H. and G. Stelmach, *Signal-to-noise ratio of handwriting size, force and time: Cues to early markers of Parkinson's disease?* , in *Sensorimotor impairment in the elderly*, G. Stelmach and V. Homberg, Editors. 1993, Kluwer Academic: Norwell, MA. p. 311-328.

81. Dutta, G., S. Freitas, and J. Scholz, *Diminished Joint Coordination with Aging leads to more variable Hand Paths.* Human Movement Science, 2013. **32**(4): p. 768-784.
82. Ketcham, C., et al., *Age-related kinematic differences as influenced by task difficulty, target size, and movement amplitude.* Journal of Gerontology, 2002. **23**: p. 1644-1664.
83. Pratt, J., A. Chasteen, and R. Abrams, *Rapid Aimed Limb Movements: Age Differences and Practice Effects in Component Submovements.* Psychology and Aging, 1994. **9**(2): p. 325-334.
84. Rey-Robert, B., et al., *Combining Movement Kinematics, Efficiency Functions, and Brinley Plots to Study Age-Related Slowing of Sensorimotor Processes: Insights from Fitt's Task.* Gerontology, 2012. **58**(2): p. 171-180.
85. Seidler-Dobrin, R., J. He, and G. Stelmach, *Coactivation to Reduce Variability in the Elderly.* Motor Control, 1998. **2**: p. 314-330.
86. Pohl, P., C. Winstein, and B. Fisher, *The Locus of Age-Related Movement Slwoing: Sensory Processing in Continuous Goal Directed Aiming.* Journal of Gerontology, 1996. **51B**(2): p. 94-102.
87. Poston, B., et al., *Movement structure in young and elderly adults during goal-directed movements of the left and right arm.* Brain and Cognition, 2009. **69**(19): p. 30-38.
88. Walker, N., D. Philbin, and A. Fisk, *Age-Related Differences in Movement Control: Adjusting Submovement Structure to Optimize Performance.* Journal of Gerontology 1997. **52B**(1): p. 40-52.
89. Kelso, J., D. Southard, and D. Goodman, *On the Nature of Human Interlimb-Coordination.* Science, 1979. **203**(4384): p. 1029-1031.
90. Stelmach, G., P. Amrhein, and N. Goggin, *Age Differences in Bimanual Coordination.* Journal of Gerontology, 1988. **43**(1): p. 18-23.
91. Birren, J. and J. Botwinick, *The relation of writing speed to age and to the senile psychoses. In: Physical dimensions of aging.* Journal of Consulting Psychology, 1951. **15**(3): p. 243-249.
92. Dixon, R., D. Kurzman, and I. Friesen, *Handwriting performance in younger and older adults: Age, familiarity, and practice effects.* Psychology and Aging, 1993. **8**: p. 360-370.
93. Slavin, M., J. Phillips, and J. Bradshaw, *Visual Cues and the Handwriting of older Adults: A kinematic Analysis.* Psychology and Aging, 1996. **11**(3): p. 521-526.
94. Spirduso, W., K. Francis, and P. MacRae, *Physical dimensions of aging*. 2005, Leeds, UK: Human Kinetics.

95. Fozard, J., et al., *Age Differences and Changes in Reaction Time: The Baltimore Longitudinal Study of Aging.* Journal of Gerontology, 1994. **49**(4): p. 179-189.
96. Juncos-Rabadán, O., A. Pereiro, and D. Facal, *Cognitive interference and aging: Insights from a spatial stiumulus-response consistency task.* Acta Psychologica, 2008. **127**: p. 237-246.
97. Bellgrove, M., et al., *Response (Re-)Programming in Aging: A Kinematic Analysis.* The Gerontological Society of America, 1998. **53A**(3): p. 222-227.
98. Ketcham, C. and G. Stelmach, *Movement Control in the Older Adult*, in *Technology for Adaptive Aging*, V.H.S. Pew RW, Editor. 2004, National Academics Press (US): Washington (DC).
99. Krampe, R., *Aging, expertise and fine motor movement.* Neuroscience and Biobehavioral Reviews, 2002. **26**: p. 769-776.
100. Salthouse, T., *The Processing-Speed Theory of Adult Age Differences in Cognition.* Psychological Review, 1996. **103**(3): p. 403-428.
101. Cabeza, R., *Hemispheric Asymmetry Reduction in Older Adults: The HAROLD Model.* Psychology and Aging, 2002. **17**(1): p. 85-100.
102. Coats, R., et al., *Eye-hand coordination strategies in older adults.* Journal of Vision, 2015. **15**(12): p. 1152.
103. Coats, R., et al., *Eye and hand movement strategies in older adults during a complex reaching task.* Experimental Brain Research, 2016. **234**(2): p. 533-547.
104. Salthouse, T., *Adutl age and the speed-accuracy trade-off.* Ergonomics, 1979. **22**(7): p. 811-821.
105. Verhaegen, P., et al., *Aging and Dual-Task Performance: A Meta-Analysis.* Psychology and Aging, 2003. **18**(3): p. 443-460.
106. Bell-McGinty, S., et al., *Standard measures of executive funtion in predicting activities of daily living in older adults.* International Journal of Geriatric Psychiatry, 2002. **17**: p. 828-834.
107. Revheim, N. and A. Medalia, *The independent living scales as a measure of functional outcome for schizophrenia.* Psychiatric Services, 2004. **55**(9): p. 1052-1054.
108. Worthington, A., *Treatments and technologies in the rehabilitation of apraxia and action disorganisation syndrome: A review.* NeuroRehabilitation, 2016. **39**(1): p. 163-174.
109. Morady, K. and G. Humphreys, *Multiple task demands in action disorganization syndrome.* Neurocase, 2011. **17**(5): p. 461-472.
110. Zwinkels, A., et al., *Assessment of apraxia: inter-rater reliability of a new apraxia tes, association between apraxia and other cognitive deficits and prevalence of apraxia in a rehabilitation setting.* Clinical Rehabilitation, 2004. **18**(7).

111. Donkervoort, M., et al., *Prevalence of apraxia among patients with a first left hemisphere stroke in rehabilitation centres and nursing homes.* Clinical Rehabilitation, 2000. **14**(2).
112. Snowden, J., D. Neary, and D. Mann, *Frontotemporal dementia.* The British Journal of Psychiatry, 2002. **290**(2): p. 140-143.
113. Edwards, D., et al., *A Quantitative Analysis of Apraxia in Senile Dementia of the Alzheimer Type: Stage-Related Differences in Prevalence and Type.* Dementia and Geriatric Cognitive Disorders, 1991. **2**(3): p. 142-149.
114. Smits, L., et al., *Apraxia in Mild Cognitive Impairment and Alzheimer's Disease: Validity and Reliability of the Van Heugten Test for Apraxia.* Dementia and Geriatric Cognitive Disorders, 2014. **38**(1-2): p. 55-64.
115. Rikli, R. and C. Jones, *Senior Fitness Test Manual*. 2009: Human Kinetics.
116. Rushmore, J., *The R-G pegboard test of finger dexterty.* Journal of Applied Psychology, 1942. **26**: p. 523-529.
117. Mathiowetz, V., et al., *Adult Norms for the Nine Hole Peg Test of Finger Dexterity.* Occupational Therapy Journal of Research, 1985. **5**(1): p. 24-38.
118. Mathiowetz, V., et al., *Adult Norms for the Box and Block Test of Manual Dexterity.* The American Journal of Occupational Therapy, 1985. **39**(6): p. 386-391.
119. Buehler, P. and E. Fuchs, *Box and Block Test*. 1957, Sammons Preston Rolyan, Inc.
120. Osness, W., et al., *Functional fitness assessment for adults over 60 years (A field based assessment)*, ed. V. Reston. 1990: American Alliance for Health, Physcial Education, Recreation and Dance.
121. Aaron, D. and C. Jansen, *Development of the Functional Dexterity Test (FDT): construction, validity, reliability, and normative data.* Journal of Hand Therapy, 2003. **16**(1): p. 12-21.
122. Jebsen, R., et al., *An objective and standardized test of hand function.* Archives of Physical Medicine and Rehabilitation, 1969. **50**: p. 311-319.
123. Hermsdörfer, J., *Bewegungsmessung zur Analyse von Handfunktionen - Vorschlag einer standardisierten Untersuchung*. EKN - Beiträge für die Rehabilitation. 2002, München.
124. Schoppe, K., *Das MLS-Gerät: ein neuer Testapparat zur Messung feinmotorischer Leistungen.* Diagnostica, 1974. **20**: p. 43-47.
125. Leuenberger, K., et al., *A method to qualitatively assess arm use in stroke survivors in the home environment.* Medical & Biological Engineering & Computing, 2017. **55**(1): p. 141-150.

126. Rand, D. and J. Eng, *Arm-Hand Use in Healthy Older Adults.* American Journal of Occupational Therapy, 2010. **64**: p. 877-885.
127. Lange, B., et al., *Development and evaluation of low cost game based balance rehabilitation tool using the microsoft kinect sensor.* Engineering in Medicine and Biology Society, EMBC, 2011 Annual International Conference of the IEEE, 2011: p. 1831-1834.
128. König, A., et al., *Ecological assessment of autonomy in instrumental activities of daily living in dementia patients by the means of an automatic video monitoring system.* Frontiers in Aging Neuroscience, 2015. **7**(98).
129. Obhi, S., *Bimanual Coordination: An Unbalanced Field of Research.* Motor Control, 2004. **8**: p. 111-120.
130. Folstein, M., S. Folstein, and P. McHuch, *Mini-Mental State (a practical method for grading the state of patients for the clinician).* Journal of Psychiatric Research, 1975. **12**: p. 189-198.
131. Reitan, R. and D. Wolfson, *The Halstead-Reitan Neuopsychological Test Battery: Therapy and clinical interpretation*. 1985, Tucson, AZ: Neuropsychological Press.
132. War Department, A.G.s.O., *Manual of Directions and Scoring*, in *Army Individual Test Battery*. 1944: Washington, DC.
133. Tombaugh, T., *Trail Making Task A and B: Normative data stratified by age and education.* Archives of Clinical Neuropsychology, 2004. **19**: p. 203-214.
134. Shulman, K., et al., *Clock-drawing and dementia in the community: A longitudinal study.* International Journal of Geriatric Psychiatry, 1993. **8**: p. 487-496.
135. Hermsdörfer, J., S. Hentze, and G. Goldenberg, *Spatial and kinematic features of apraxic movement depend on the mode of execution.* Neuropsychologia, 2006. **44**: p. 1642-1652.
136. Hermsdörfer, J., et al., *Tool use without a tool: kinematic characteristics of pantomiming as compared to actual use and the effect of brain damage.* Experimental Brain Research, 2012. **218**(2): p. 201-214.
137. Hermsdörfer, J., et al., *Tool use kinematics across different modes of execution.* Cortex, 2013. **49**: p. 184-199.
138. Hermsdörfer, J., et al., *Kinematic analysis of movement imitation in apraxia.* Brain, 1996. **119**(5): p. 1575-1586.
139. Woytowicz, E., J. Whitall, and K. Westlake, *Age-related Changes in Bilateral Upper Extremity Coordination.* Current Geriatric Reports, 2016. **5**(3): p. 191-199.
140. Shirota, C., et al., *On the assessment of coordination between upper extremities: towards a common language between rehabilitation*

engineers, clinicians and neuroscientists. Journal of NeuroEngineering and Rehabilitation, 2016. **13**(80).
141. Wood, R., *Task Complexity: Definition of the Construct.* Organizational Behavior and Human Decision Processes, 1986. **37**: p. 60-82.
142. Eidenmüller, S., et al., *The impact of unilateral brain damage on anticipatory grip force scaling when lifting everyday objects.* Neuropsychologia, 2014. **61**: p. 222-234.
143. Wu, C.-Y., et al., *Effects of Modified Constraint-Induced Movement Therapy on Movement Kinematics and Daily Function in Patients with Stroke: A Kinematic Study of Motor Control Mechanisms.* Neurorehabilitation and Neural Repair, 2007. **21**: p. 460.
144. Naylor, J. and T. Dickinson, *Task structure, work structure, and team performance.* Journal of Applied Psychology, 1969. **53**: p. 167-177.
145. Gulde, P. and J. Hermsdörfer, *Both hands at work: The effect of aging on upper-limb kinematics in a multi-step activity of daily living.* Experimental Brain Research, 2017. **235**(5): p. 1337-1348.
146. Gulde, P., C. Hughes, and J. Hermsdörfer, *Effects of Stroke on Ipsilesional End-Effector Kinematics in a Multi-Step Activity of Daily Living.* Frontiers in Human Neuroscience, 2017. **11**(42).
147. Hermsdörfer, J., et al., *Effects of unilateral brain damage on grip selection, coordination, and kinematics of ipsilesional prehension.* Experimental Brain Research, 1999. **128**(1-2): p. 41-51.
148. Godefroy, O., et al., *Stroke and Action Slowing: Mechanisms, Determinants and Prognosis Value.* Cerebrovascular Diseases, 2010. **29**: p. 508-514.
149. Romero, D., et al., *Altered aiming movements in Parkinson's disease patients and elderly adults as a function of delays in movement onset.* Experimental Brain Research, 2003. **151**: p. 249-261.
150. Schaefer, S., K. Haaland, and R. Sainburg, *Hemispheric Specialization and Functional Impact of Ipsilesional Deficits in Movement Coordination and Accuracy.* Neuropsychologia, 2009. **47**(13): p. 2953-2966.
151. Gorus, E., et al., *Reaction times and performance variability in normal aging, mild cognitive impariemtn, and Alzheimer's disease.* Journal of Geriatric Psychiatry and Neurology, 2008. **21**(3).
152. Dykiert, D., et al., *Age Differences in Intra-Individual Variability in Simple and Choice Reaction Time: Systematic Review and Meta-Analysis.* PLoS One, 2012. **7**(10).

153. Bailey, R., J. Klaesner, and C. Lang, *Quantifying Real-World Upper-Limb Activity in Nondisabled Adults and Adults With Chronic Stroke.* Neurorehabilitation and Neural Repair, 2015. **1**(10).
154. Lewis, G. and W. Byblow, *Bimanual Coordination Dynamics in Poststroke Hemiparetics.* Journal of Motor Behavior, 2004. **36**(2): p. 174-188.
155. Metrot, J., et al., *Changes in Bimanual Coordination During the First 6 Weeks After Moderate Hemiparetic Stroke.* Neurorehabilitation and Neural Repair, 2013. **27**(3): p. 251-259.
156. Bailey, R. and C. Lang, *Upper extremity activity in adults: Referent values using accelerometry.* Journal of Rehabilitation Research & Development, 2014. **50**(-): p. 1213-1222.
157. Maes, C., et al., *Two hands, one brain, and aging.* Neuroscience & Biobehavioral Reviews, 2017. **75**: p. 234-256.
158. Ramanujan, S. 1914.
159. Rohrer, B., et al., *Movement Smoothness Changes during Stroke Recovery.* The Journal of Neuroscience, 2002. **22**(18): p. 8297-8304.
160. Hughes, C., et al., *The application of SHERPA (Systematic Human Error Reduction and Prediction Approach) in the development of compensatory cognitive rehabilitation strategies for stroke patients with left and right brain damage.* Ergonomics, 2014.
161. Schwartz, A., et al., *Analysis of a disorder of everyday action.* Cognitive Neuropsychology, 1995. **12**(8): p. 863-892.
162. Flash, T. and E. Henis, *Arm Trajectory Modifications During Reaching Towards Visual Targets.* Journal of Cognitive Neuroscience, 1991. **3**(3).
163. Gulde, P. and J. Hermsdörfer, *A comparison of smoothing a filtering approaches using simulated kinematic data of human movements*. Proceedings of the 11th international Symposium on Computer Science in Sport (IACSS 2017) ed. Advances in Intelligent Systems and Computing. Vol. 663. 2018: Springer, Cham.
164. Gulde, P., et al., *Introduction of the reciprocal trail making task for the assessment of ADL performance in patients with MCI, dementia, PTSD and AD*. 2017, dvs Sektion Sportmotorik: Augsburg. p. 54-56.
165. Bailey, R., R. Birkenmeier, and C. Lang, *Real-World Affected Upper Limb Activity in Chronic Stroke: An Examination of Potential Modifying Factors.* Topics in Stroke Rehabilitation, 2015. **22**(1): p. 126-33.