Development of computer-based tasks for patients with unilateral right-hemispheric neglect

A study to examine the degree of automation through velocity and acceleration on healthy participants

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Abstract

Unilateral right-hemispheric neglect is one of the most common neuropsychological diseases as a condition after a stroke. It is characterized by the negligence of one half of perception without consciously noticing it, with the possible additional involvement of motor neglect. There are still contradictory opinions about whether it is caused solely by a shift of attention or if motor deficiencies – even within the ipsilesional space – are always involved. Computer-based assessments offer further insights about this question as they provide dynamic measurements such as velocity and acceleration every few milliseconds and not only the response time of the task itself. An efficient measurement to test for potential deficiencies is the degree of automation. This study develops novel tablet-based tasks to diagnose neglect patients, which are evaluated in respects of automation and other important parameters like peak velocity, peak acceleration, and number of inversions in velocity (NIV) on healthy participants to identify potential influencing factors. The velocity and acceleration profile of every person should be normally distributed. It is expected that the dependent variables peak velocity, peak acceleration, and NIV are influenced by the extent of education and frequency of writing, but not by gender and age when conducting a task of wave drawing. While drawing horizontal lines, peak velocity is expected to differ between line direction but neither between age groups nor gender. The aim of this study is to develop novel computer-based tasks and to establish reference values for future clinical trials. 51 subjects conducted 23 tasks with the dominant right hand and 19 tasks with the left hand on a graphical Wacom tablet. For the task of wave drawing, every person's velocity and acceleration profile is investigated regarding normality with the Shapiro-Wilks test, a probability density function, and a Q-Q plot. Furthermore, a multivariate linear regression is conducted to investigate the influence of gender, age, years of education, and writing frequency on the dependent variables peak velocity, peak acceleration and NIV. The evaluation of horizontal line drawing is examined with a repeated measures ANOVA to test differences in line direction. The velocity and acceleration profiles are not sufficiently normally distributed for individuals and skewed to the left over all subjects with a long tail to the right. Neither of the independent variables have any influence on velocity, acceleration or NIV, whereas the ANOVA shows a significant difference in line direction between leftward and rightward lines. The deviations from a Gaussian distribution might be best explained by the frequently described skewness of response times, as velocity is a function of response time. The tablet-based tasks should be further modified after clinical trials to make sure there is a high sensitivity even with this small number of tasks. Since there are no notable influencing factors, it can be used for neglect patients independent of their demographics for future clinical trials. This study paves the way for clinical use, where it might potentially increase diagnostic sensitivity considerably. Furthermore, it might provide insights about its cause as well as further differentiation between motor and non-motor symptoms.

Keywords: Visuo-spatial neglect; Computer-based drawing analysis; Automation of drawing; Neglect assessment

Zusammenfassung

Unilateraler rechts hemisphärischer Neglect ist eine der häufigsten neuropsychologischen Erkrankungen nach einem Schlaganfall. Neglect ist durch die unbewusste Vernachlässigung einer Wahrnehmungshälfte gekennzeichnet, mit der möglichen zusätzlichen Beteiligung von motorischem Neglect. Es gibt nach wie vor widersprüchliche Meinungen darüber, ob Neglect allein durch eine Verlagerung der Aufmerksamkeit verursacht wird oder ob auch innerhalb des ipsiläsionalen Raumes immer motorische Defizite involviert sind. Computergestützte Assessments könnten tiefere Erkenntnisse zu dieser Frage liefern, da dabei beispielsweise alle paar Millisekunden dynamische Parameter wie Geschwindigkeit und Beschleunigung gemessen werden und nicht nur die Reaktionszeit der Aufgabe selbst. Eine effiziente Messung zur Prüfung auf potentielle Defizite ist der Automatisierungsgrad. In dieser Studie werden neuartige tablet-basierte Aufgaben zur Diagnose von Neglect Patienten entwickelt, die in Bezug auf den Automatisierungsgrad und andere wichtige Parameter wie Höchstgeschwindigkeit, Spitzenbeschleunigung und Anzahl der Geschwindigkeitsinversionen (NIV) bei gesunden Teilnehmern ausgewertet werden, um potenzielle Einflussfaktoren zu identifizieren. Das Geschwindigkeits- und Beschleunigungsprofil jeder Person sollte normalverteilt sein. Es wird beim Wellenzeichnen erwartet, dass die abhängigen Variablen Höchstgeschwindigkeit, Spitzenbeschleunigung und NIV von der Dauer der Ausbildung und der Häufigkeit des Schreibens nicht aber von Geschlecht und Alter beeinflusst werden. Beim Zeichnen horizontaler Linien wird erwartet, dass sich die Höchstgeschwindigkeit je nach Linienrichtung aber weder zwischen den Altersgruppen noch zwischen dem Geschlecht unterscheidet. Das Ziel dieser Studie ist es, neuartige computergestützte Aufgaben zu entwickeln und Referenzwerte für zukünftige klinische Studien zu erheben. 51 Probanden führten 23 Aufgaben mit der dominanten rechten Hand und 19 Aufgaben mit der linken Hand auf einem graphischen Wacom Tablet durch. Für die Aufgabe des Wellenzeichnens wird das Geschwindigkeits- und Beschleunigungsprofil jeder

Person hinsichtlich Normalverteilung mithilfe des Shapiro-Wilks-Tests, einer Wahrscheinlichkeitsdichtefunktion und einem Q-Q-Plot untersucht. Darüber hinaus wird eine multivariate lineare Regression durchgeführt, um den Einfluss von Geschlecht, Alter, Bildungsjahren und Schreibhäufigkeit auf die Regressanden Höchstgeschwindigkeit, Spitzenbeschleunigung und NIV zu untersuchen. Die Auswertung des horizontalen Linienzeichnens wird durch eine ANOVA mit Messwiederholung untersucht, um Unterschiede in der Linienrichtung zu testen. Die Geschwindigkeits- und Beschleunigungsprofile sind für alle Probanden nicht ausreichend normalverteilt sondern linkssteil. Keine der unabhängigen Variablen hat irgendeinen Einfluss auf die Geschwindigkeit, Beschleunigung oder NIV, während die ANOVA einen signifikanten Unterschied in der Linienrichtung zwischen links- und rechtsgerichteten Linien aufzeigt. Die Abweichungen von der Gaußschen Verteilung lassen sich möglicherweise durch die häufig beschriebene Schiefe der Antwortzeiten erklären, da die Geschwindigkeit eine Funktion der Antwortzeit ist. Die tablet-basierten Aufgaben sollten nach ersten klinischen Studien weiter modifiziert werden, um sicherzustellen, dass auch bei dieser kleinen Anzahl von Aufgaben eine hohe Sensitivität gegeben ist. Da es keine nennenswerten Einflussfaktoren gibt, können die Aufgaben für Neglect Patienten unabhängig ihrer Demographie für zukünftige klinische Studien verwendet werden. Diese Studie ebnet den Weg für den klinischen Einsatz, wo sie die diagnostische Sensitivität möglicherweise erheblich steigern könnte. Darüber hinaus könnten neue Erkenntnisse über die Ursachen sowie weitere Differenzierungen zwischen motorischen und nicht-motorischen Symptomen gewonnen werden.

Schlüsselwörter: Visuell-räumliches Neglect; Computerbasierte Zeichnungsanalyse; Automatisierung des Zeichnens; Neglect Erfassung

Contents

1 Introduction

The frequency of neurological and neuropsychological diseases, especially those involving brain damage, increased in recent years. One of the most common diseases is called neglect, which often appears as a condition after a stroke. It is characterized by the negligence of one half of perception without consciously noticing it, with the possible additional involvement of motor neglect. In the latter, the patients use one body half less than the other, which cannot be explained by the paresis. Thus, it is a burdening state for the affected persons. It results in a lot of restrictions in everyday life such as only eating half of the plate or exposing oneself to danger when crossing a regular intersection as well as worsen the prognosis of rehabilitation after a stroke meaningfully. Although there has been a lot of research about the origin of neglect, there are still contradictory opinions about whether it is just a shift of attention in general or if there are additional deficiencies even within the perceivable visual area itself involved. More precisely, do patients with spatial neglect and without motor neglect show motion deficiencies in the half of space, where they are hypothesized to function normal? Are motor deficiencies always involved with spatial neglect? What might these disabilities look like and how do they differ?

A reason those questions have not been answered yet is partly due to insufficient measurement tools, as the standards for diagnostics and research are pen-and-paper tests, which only measure static parameters like the number of line bisections or response time. Recent progress in the context of digitization offers entirely new approaches by providing information about the process, i.e. not only is response time measured but various dynamic parameters such as velocity during the whole movement profile over the course of the task. An example would be a task of drawing waves on a graphical tablet. The computerized procedures might also enhance the diagnostic sensitivity in comparison to their analogue counterparts, which, inter alia, overlook mild forms and lack sufficient differentiation. One way to measure deficits in motor processes is due to the degree of movement automation, which is best captured through the velocity and acceleration profile in hand-writing and drawing. If there are limitations in movement automation, it could indicate deficiencies within motor areas. Furthermore, peak velocity and peak acceleration might underpin those insights indirectly. If muscles or their innervating nerves are damaged, peak velocity and acceleration are expected to decrease, leading to insufficient movements and flawed hand-writing or drawings.

This study focuses on developing novel tablet-based diagnostic tasks for neglect patients to answer these questions about the cause of neglect and to further differentiate between its motor and non-motor symptoms. To develop new diagnostic tasks, they have to be evaluated on healthy participants first. This work measures reference values of a healthy control group and thus can be viewed as a pre-study for future clinical trials. Furthermore, potentially influencing factors, which might have to be considered as confounding variables are investigated. In the following, the theoretical background of neglect with its symptoms and anatomical foundations, its current diagnostic process and treatment with or without computer-based methods as well as the automation of hand-writing and drawing tasks with differences due to visual feedback are elaborated in detail.

1.1 Unilateral right-hemispheric neglect

Spatial neglect is one of the most common neuropsychological diseases after vascular brain accidents (Pedroli et al., 2015). It is caused by brain damage in the form of a lesion, usually as a condition after a stroke (Karnath, 2012). The frequency of brain damage is increasing with a growing tendency, which makes the diagnosis and rehabilitation of neglect more important. Furthermore, damages in the right-hemisphere after a stroke are accompanied by neglect in 43% of the cases (Obo, Adachi & Kubota, 2017; Ringman, Saver, Woolson, Clarke & Adams, 2004). Although neglect is most often found in adults, it can also be observed in children (Laurent-Vannier, Pradat-Diehl, Chevignard, Abada & De Agostini, 2003). There are two kinds of unilateral spatial neglect, depending on whether the location of the lesion is either in the right or left hemisphere. Unilateral means that the damage is located on one hemisphere exclusively. Unilateral right-hemispheric neglect describes a lesion in the right hemisphere, which results in spatial deficits on the left side of space. *Unilateral right-hemispheric neglect* will be referred to as *neglect* consistently throughout this paper. The choice of the right hemisphere as a focus results in its far more prevalent appearance than its left equivalent and because it leads to more severe symptoms (e.g. Ringman et al., 2004; Stone et al., 1991; Vallar & Perani, 1986). A special characteristic of neglect is that the deficits in the visual and motor system cannot be explained anatomically. Thus, neglect can be described as a problem of attention not perception. However, experimental studies show that patients perceive the stimuli implicitly in the contralesional field but do not process them consciously (Goldenberg, 2017).

The specific underlying mechanisms need yet to be fully understood though. There are various hypotheses about the origin of neglect. According to Goldenberg (2017), it might be caused by generally decreased attention. More specifically, Karnath (2012) discusses three different hypotheses, which focus on attention, representation, and transformation. The *attention theory* proposes a deficiency of disengaging from an ipsilesional stimulus in favor of a contralesional one (Posner, Walker, Friedrich & Rafal, 1987). This then leads to increased attention within the ipsilesional area. More precisely, neglect might be due to deficits within any of the three parts of the attention process: disengagement, shift or movement and engagement. The *representation hypothesis* presumes an incorrect mental representation of the stimulus, leading to a compression of the perceivable area (e.g. Bisiach, Capitani, Luzzatti & Perani, 1981; Halligan & Marshall, 1991). Depending on the authors, either a uniform or a gradually increasing compression is proposed. Karnath (2012) argues that the most probable theory is the *transformation hypothesis*, which assumes a disrupted neuronal transformation of the multimodal sensor implementation of mental representations. It causes a rotation in the vertical body axis of the earth and thus an increased focus of attention to the ipsilesional side (e.g. Karnath, 1994, 1997; Pouget & Driver, 2000). All three hypotheses imply that perception itself is not impaired within this one side of space. According to those hypotheses, neglect patients should not have motor or non-motor deficits within the ipsilesional side. However, this remains unproven.

1.1.1 Symptoms

There are various symptoms caused by neglect, which have to be subdivided into egocentric (relative to the body of the individual) and allocentric (object-centered) symptoms (Karnath & Rorden, 2012). According to Karnath and Rorden (2012), the former is the core deficit in spatial neglect and thus the focus of this study. For example, object-centered deficits (e.g. as observable in cancellation tasks) can only be found in 40% of the neglect patients (Karnath & Rorden, 2012). Note that neglect has to be differentiated diagnostically in particular from hemianopsia (Goldenberg, 2017) and anosognosia (Appelros, Karlsson & Hennerdal, 2007; Heilman, Valenstein & Watson, 1984) as their symptoms can overlap, especially in the acute phase of neglect. One central question regarding the symptoms is whether it is only a shift of the center of spatial exploration or if there are deficiencies within the ipsilesional side of perception, additionally. The literature is not conclusive regarding the answer to this question. Although there are hints for deficiencies beside the negligence of the left side, the focus of neglect as a pathology is mainly on the shifted center of spatial exploration (Karnath, 2012). Symptoms can be subdivided into motor neglect such as directional hypokinesia, motor extinction, and motoric impersistence as well as non-motor symptoms like sensory-attentional neglect, misperception, hyper rightward attention, and failure of shifting attention (Chiba & Haga, 2008; Laplane & Degos, 1983).

Motor symptoms. Compared to healthy subjects, unilateral right-hemispheric neglect patients have an asymmetric movement execution, i.e. they tend to deviate to the ipsilesional right side. One such characteristic is that they underestimate left-sided and overestimate right-sided stimuli (e.g. Charras et al., 2012; Hacke & Poeck, 2015; Karnath, 2012). Mattingley, Phillips and Bradshaw (1994) state that the execution time of different tasks is slower the more severe the diagnosed neglect. Another explanation is the presence of concurring motor programs when interpreting irrelevant ipsilesional stimuli (Goldenberg, Münsinger & Karnath, 2009; Mattingley et al., 1998). Neglect patients also tend to lean towards the ipsilesional side with their entire body (Karnath, 2012). Additionally, less efficient motion execution can be quantified by slower leftward lines than rightward, where – aside from the difference in response time – a less bell-shaped profile of velocity can be observed (Mattingley et al., 1994). For unpredictable movements and contralesional stimuli with concurrent ipsilesional distractors the execution time decreases (Mattingley et al., 1998). This might support the *attention hypothesis* described in section 1.1 because those findings imply problems with the disengagement from the current, ipsilesional stimuli. The ability to imitate gestures with the finger compared to gestures with entire the hand is decreased, although this depends on the severity (Goldenberg et al., 2009). This might be viewed as a special form of apraxia.

Non-motor symptoms. The shift of attention might be separated into object (allocentric) and space (egocentric) centered, meaning that the neglect of the left side is present when the focus of attention applies to the whole room as well as when one object within the room is being focused on (Karnath, 2012). Hence, at least parts of the object's left side will be neglected, too. An overall reduced capacity for the process of visual information can be observed as well as reduced attention (Goldenberg et al., 2009; Hacke & Poeck, 2015). According to Goldenberg (2017), not only the visuo-spatial working memory is limited but also the figurative imagination. Alertness is modulated worse without intervention, though it can be manipulated for the better through a stimulus. Therefore, the phasic alertness increases, leading to decreased deficiencies on the left, contralesional side for a short period of time (Chica et al., 2012; Malhotra, Coulthard & Husain, 2009).

1.1.2 Neglect's anatomy

The location of the lesion which causes unilateral right-hemispheric visuo-spatial neglect is in the right hemisphere. There has been a lot of discussion about the exact areas within the right hemisphere and inconsistent results in the literature over time. Recent research proposes an impairment of the so called perisylvic cortical system, which consists of three components (Karnath, 2012). One region is the superior and middle temporal gyrus with its adjacent insular lobe (Cappa, Guariglia, Messa, Pizzamiglio & Zoccolotti, 1991; Karnath, 2012; Karnath & Rorden, 2012) and another is the ventrolateral prefrontal cortex (Karnath, 2012; Karnath & Rorden, 2012). The third region within the perisylvic system is the inferior parietal lobe (Cappa et al., 1991; Hacke & Poeck, 2015; Karnath, 2012; Vallar & Perani, 1986) or more specifically, its ventral attention network which contains the angular and the supramarginal gyrus (Mort et al., 2003; Toba et al., 2018). In addition to lesions within the cortical regions, lesions in subcortical regions can cause or worsen the neglect, too. More precisely, the putamen and less often the caudate nucleus as part of the basal ganglia and the pulvinar as part of the thalamus are affected (Hacke & Poeck, 2015; Karnath, 2012; Vallar & Perani, 1986). Goldenberg (2017) states the effect of a lesion within those areas should be similar to frontal lesions. Thus, he suggests that it is not the neurons within these subcortical areas themselves that cause the deficits of unilateral attention. The source is rather the remote effect on the cortical regions described earlier, because damages in those subcortial regions reduce the metabolism and hence their functionality. Not only gray matter is important but also the pathways consisting of white matter, which connect the perisylvic system. The inferior longitudinal fasciculus, arcuate fasciculus, and extreme capsule connect the superior and middle temporal gyrus with the ventrolateral prefrontal cortex, while the superior longitudinal fasciculus and the superior occipito-frontal fasciculus connect the ventro-lateral prefrontal lobe with the inferior parietal lobe (Karnath, Rüter, Mandler & Himmelbach, 2009). Damages within the white matter, which lead to a disconnection, play an important role e.g. for visual neglect (Doricchi, de Schotten, Tomaiuolo & Bartolomeo, 2008).

According to Karnath (2012) as well as Karnath, Ferber and Himmelbach (2001), the superior and middle temporal cortex are the most critical areas for lesions after a stroke causing neglect, since they are mainly responsible for spatial orientation with a dominant effect in the right hemisphere. On the other hand, Malhotra et al. (2009) emphasize the role of the posterior parietal cortex for spatial orientation instead, while Mort et al. (2003) only found lesions of the superior temporal gyrus in half of the patients. Goldenberg (2017) argues that the variety of neuroanatomical areas is caused by their task-specificity, e.g. sensoric neglect of one site is caused by lesions within the temporal cortex or the temporo-parietal transition area and the preference for one direction of action is caused by frontal lesions. Toba et al. (2018) proposes that only the angular and supramarginal gyrus are generally involved and all other regions only show task specific damage. According to Karnath and Rorden (2012), these inconsistencies in literature are the result of inaccurate use of the term spatial neglect in recent years, where the term has increasingly been misused in a broader context.

1.1.3 Diagnostic process

According to Menon-Nair, Korner-Bitensky, Wood-Dauphinee and Robertson (2006), neglect is not typically assessed after an acute stroke as a standardized procedure. If it is assessed in clinical practice, a bedside pen-and-paper test, such as cancellation tasks, is usually conducted in order to classify the severity of neglect in two (absent, neglect) or four categories (absent, mild, moderate, severe) (e.g. Ishiai, 1994; Liang, Fairhurst, Guest & Potter, 2010; Tsirlin, Dupierrix, Chokron, Coquillart & Ohlmann, 2009). Various neuropsychological test procedures have been proposed. The most used pen-and-paper test – the Rivermead Behavioral Inattention Test (BIT) – uses former categorization and consists of 15 subtests divided into two sections. On the one side, nine performance-based, *behavioral* subtests like dialing a phone and other everyday life tasks, such as menu-reading, map reading are evaluated (Halligan, Cockburn & Wilson, 1991; Wilson, Cockburn & Halligan, 1987). The remaining six subtests contain more *conventional* tasks like line crossing, letter and star cancellation, figure, and shape copying, line bisection, and representational drawing. Although the well-known BIT has acceptable sensibility (Azouvi et al., 2002; Halligan, Marshall & Wade, 1989) and validity (Hartman-Maeir & Katz, 1995), it lacks certain aspects compared to computer-based assessments, which are discussed in section 1.1.5. Other tests mostly adopt parts or variations of the items used in the frame of the BIT (e.g. Azouvi et al., 2002; Cherney, Halper, Kwasnica, Harvey & Zhang, 2001; O'Reilly & Plamondon, 2014; Rorden & Karnath, 2010). Another widely used screening instrument is the computerized Test Battery of Attentional Performance (TAP) (Zimmermann & Fimm, 1995). It contains subtests for *alertness*, *neglect*, *visual field*, and *visual scanning*, which can be used to diagnose neglect (Thimm, Fink, Küst, Karbe & Sturm, 2006). For the former, patients have to react as fast as possible to a visual stimulus. For the latter three tests, patients have to press a key if a stimulus is shown in an area around a central square (either with or without distractors). Those three subtests differ only slightly as described by Thimm et al. (2006).

Recently, novel approaches have been introduced. For example, Brink, Visser-Meily and Nijboer (2018) propose a dynamic diagnostic tool called Mobility Assessment Course, where patients have to walk through a predefined route on which they have to find and report 24 targets on the walls. In the future, eye-tracking could add diagnostic value to existing test batteries. Kaufmann et al. (2020) found less fixations and less time spent within the left field of view and more fixations and time spent in the right field of view compared to healthy participants. Additionally, eye-tracking measured a decreased visual exploration in the left, but the same exploration in the right area. The study also suggests that neglect patients have a decreased efficiency, measured by more overlapping fixations on the right side. This serves as an example for additional information provided by computer-based diagnostic tools as described and introduced in section 1.1.5 and 1.3 of this work. Note that since there are little to no concurring stimuli in a clinical setting, the symptoms will most likely be larger in the patient's daily life (Goldenberg, 2017). Thus, screening procedures have to be sensitive and one has to be aware of the differences in clinical settings to get an approximate idea of the real circumstances and burdens that accompany it for the patient.

1.1.4 Treatment and rehabilitation

Rehabilitation after a right-hemispheric stroke takes longer with a severe neglect than one of lower severity (e.g. Cappa et al., 1991; Cherney et al., 2001; Chica et al., 2012). It is important to continuously enhance the quality and efficiency of treatment and rehabilitation. According to Karnath, Rennig, Johannsen and Rorden (2011), there are frequent spontaneous remissions within the first week up to a few months. Furthermore, certain treatments are available, which can improve the symptoms of neglect and therefore lead to a more promising rehabilitation (Karnath et al., 2011). Note that the long-term effects of those interventions and exercises are still controversial. The theoretical basis behind the treatments is most often a repeated short-term reaction, which should lead to a long-term adaption eventually. For example, striking reference stimuli to the contralesional side – which are called *cueing* – massively improve short-term perceptual performance (Karnath, 2012). This can be called a bottom-up process. Note that the chosen treatment and rehabilitation strongly depends upon the opinion about the cause of neglect as described by the different hypotheses in section 1.1. A dynamic background where stripes move to the contralesional side inevitably leads to an eye movement to the left side (Goldenberg, 2017). One could also stimulate the vestibular system with either neck vibration on the left side or flushing cold water in the left ear, since both lead to an eye movement to the contralesional (left) side (Tsirlin et al., 2009), although the latter should be avoided as it may lead to nausea. Auditory stimulation improves general alertness and can hence be described as a top-down process (Karnath, 2012; Tsirlin et al., 2009).

Another option is optokinetic stimulation, where visual stimuli move e.g. from the right to the left (Tsirlin et al., 2009). According to Kerkhoff (1998), the best method is to mask one half of each eye, resulting in a reduction of the input recorded by the contralesional superior colliculus. Therefore, the ipsilesional colliculus shows an increased effectiveness and in further consequence leads to more eye movements to the contralesional field of vision. Tsirlin et al. (2009) argue that the most effective rehabilitation method is the prism adaption, which leads to a lateralized reorganization in visuo-motor mapping (Luaute, Halligan, Rode, Jacquin-Courtois & Boisson, 2006; Smit et al., 2013). It can be carried out with prism glasses, causing an extra relocation of the field of vision. The idea is that the patients look through the prism glasses and the visual field appears to be more to the right than usual. If the glasses are taken off, they should keep this relocation and hence look more to the left. This is caused by a lateral shift of the visual field as the target appears at a new and displaced location because of the prism glasses (Luaute et al., 2006; Serino, Barbiani, Rinaldesi & Ladavas, 2009). Significant improvements can be achieved through training of spatial and visual exploration and visual orientation discrimination (Karnath, 2012; Kerkhoff, 1998; Tsirlin et al., 2009).

There have been attempts to perform the visuo-spatial and exploration tasks in virtual reality (e.g. Tsirlin et al., 2009; Yasuda, Muroi, Ohira & Iwata, 2017). Recent approaches integrated computer-based methods to create a rehabilitation support system, which consists of a so-called computational system rehabilitation with additional motion measurement. For example, Obo et al. (2017) implemented a task battery on a tablet PC with appearing circular objects, which move from one side to the other and giving the patient three seconds to touch the circle. There has not been much reliable research regarding a pharmacological therapy of neglect. Only cholinergic drugs provide at least some evidence to improve the symptoms (van der Kemp, Dorresteijn, Ten Brink, Nijboer & Visser-Meily, 2017).

1.1.5 Computer-based assessment

Since neglect prolongs the rehabilitation after a stroke, efficient diagnostic tools and rehabilitation assessments are indispensable. The typically used pen-and-paper (PnP) tests have various limitations. The measurements are only static, providing just information about the outcome in form of a score instead of the entire process, ignoring the variance within the task itself (Bonato & Deouell, 2013; Liang, Fairhurst et al., 2010). They are more difficult to change between examinations, which leads to an early normalization of the subject's scores during continuous rehabilitation assessments and therefore are not suitable for test-retest designs (Bonato & Deouell, 2013). Another shortcoming is the need for a trained examiner whose judgment has an unavoidable subjective component (Bonato & Deouell, 2013; Liang, Fairhurst et al., 2010; Liang, Guest, Fairhurst & Potter, 2007). It has repeatedly been described that PnP tests overlook light neglect symptoms, making them tests only a sufficient measure in acutes phases (Bonato & Deouell, 2013; Bonato, Priftis, Umiltà & Zorzi, 2013). Bonato et al. (2013) compared cancellation tasks with computer-based tasks, where patients had to detect lateralized targets. While the cancellations-tasks did not reveal any significant ipsilesional bias, the computer-based test did. This might be due to compensatory mechanism in cancellations-tasks, which are more difficult to apply in computer-based tasks. Hence, the sensitivity of analogue test batteries is not sufficient in comparison to their digital counterparts (Guest & Fairhurst, 2002). Smit et al. (2013) state that computer-based assessments increase the feasibility and reliability. According to Bonato and Deouell (2013) and Bonato et al. (2013), computerized tests decrease the frequency of false-negatives, i.e. patients with a mild form of neglect are less often classified as non-pathological. There are, however, also contradictory results. Early research, where the efficiency of pen-and-paper tests was compared to computer-based tests, suggested no difference between the two (Bergego et al., 1997). While there has been various research in computer-based applications for other neurological or neuropsychological diseases in the past, e.g. in the context of dysgraphia (Asselborn et al., 2018) or Parkinson's disease (e.g. Akyol, 2017; Aly, Playfer, Smith & Halliday, 2007; Drotár et al., 2016; Isenkul, Sakar & Kursun, 2014), there has not been much research on computer-based assessment in the context of neglect. In addition, the published applications of those tests are rarely built for diagnostic purposes but for research instead (Bonato & Deouell, 2013).

Computer-based assessments describe a diverse field of applications and hence there is the need to differentiate. Most of the papers describe some kind of digitization of traditional PnP test batteries, but there have been some innovative efforts, too. Obo et al. (2017) introduce an additional component of motion recording and evaluation, providing a concurrent measurement of the motor and behavioral symptoms of neglect patients. There have also been attempts to create virtual reality applications for neglect patients (Pedroli et al., 2015; Tsirlin et al., 2009; Yasuda et al., 2017) or to investigate neglect with eye tracking (e.g. Delazer, Sojer, Ellmerer, Boehme & Benke, 2018; Kaufmann et al., 2020). In the following work, the focus lies on tasks developed by a research group at the University of Kent, which introduced different approaches to computerize traditional diagnostic tools like the BIT and evaluate their most important components to efficiently assess the severity of neglect. As Donnelly et al. (1999) argue, dynamic values provide additional diagnostic information in form of temporal (premovement, movement) and strategic (start points, intersection) information during a cancellation task. This is caused by the fact that damages within the parietal lobe predict deficits in premovement or movement more frequently than without damages within said cortical area (Donnelly et al., 1999). Thus, the underlying principles of neglect in general can be investigated more thoroughly (Potter et al., 2000). For figure completion and geometric shape copying tasks, a higher sensitivity can be observed (Guest, Fairhurst & Potter, 2002; Guest, Fairhurst, Potter & Donnelly, 2000), but according to Guest and Fairhurst (2002), stand-alone dynamic process variables do not contain as much information as static parameters in cancellation tasks – meaning, they do not predict the existence of neglect as well. In those studies, participants had to copy a certain cross on a graphical tablet. Parameters like width and height (increased), total drawing distance (decreased), mean reference positional error (increased), overall execution time (increased), mean velocity (decreased), and pen lifts (increased) were extracted (Guest & Fairhurst, 2002). Note that according to Guest and Fairhurst (2002) the information degree of static parameters can be approximated through a multilevel classification or a combination of both static and dynamic information.

Chindaro, Guest, Fairhurst and Potter (2004) used Hidden Markov Models and different classifiers to elaborate on the question, which assessed variable predicts the severity of neglect most accurately and found the response time of drawing geometric figures as the result. Fairhurst et al. (2008) introduce a generic approach for tablet-based assessments with a program called MEDDRAW, to generalize the principles to various neurological or neuropsychological disorders. Liang et al. (2007) computerized, inter alia, Albert's cancellation test to train a logistic regression model to predict the binary diagnosis neglect versus healthy. Through this pattern analysis a not normal distributed cancellation time was found. Liang, Fairhurst et al. (2010) elaborate on this idea by creating a four-point scale for the severity of neglect. Again, the diagnosis according to parts of the BIT was compared to the algorithmic prediction, where they found a match of up to 92.5%. Only five of the 14 tests of the BIT are necessary because the other nine do not provide any additional information. The most important parameters are the number of cancellations in the left down quadrant, peak velocity, mean value of acceleration of the pen movement, movement time in the bottom left quadrant, height of drawing, and the ratio of pen-down to pen-up time (Liang, Fairhurst et al., 2010; Liang, Guest, Fairhurst & Potter, 2010). Hence, computer-based tests might be less time-consuming, saving up to a quarter of the duration compared to their PnP counterpart, caused by the reduced test battery size (Liang, Guest et al., 2010; Potter et al., 2000). In addition, more frequent repetitions are possible due to the patient's reduced fatigue. Another advantage is the objective and automated evaluation. However, the implementation of computerized testing is time consuming in clinical practice and often – especially in acute phases right after a stroke – not possible. Furthermore, the unique observation of the patient during PnP tests is lost, if their digital equivalent is not a similar computer-based version of itself, like proposed in section 1.3.

1.2 Automation of hand-writing and drawing

An efficient way to measure the degree of automation in hand-writing and drawing is through the velocity and acceleration profile (e.g. Eichhorn et al., 1996; Mai & Marquardt, 2014; Rueckriegel et al., 2008; Schoemaker, Ketelaars, Van Zonneveld, Minderaa & Mulder, 2005; Tigges et al., 2000). If the velocity and acceleration profile is normally distributed (i.e. bell-shaped), the movement is highly automated and smooth (Rueckriegel et al., 2008). Another parameter to quantify the degree of automation is the number of inversions in velocity (NIV). If the NIV equals to one, there is only one local maximum within the velocity distribution – the larger the value of NIV, the less automated the movement (disturbance of automation). Those parameters have been successfully used to research automation deficiencies within patients with schizophrenia, ADHD or Parkinson's disease (Eichhorn et al., 1996; Schoemaker et al., 2005; Tigges et al., 2000). For those three diseases, movement automation decreases meaningfully. Thus, similar results would be expected for neglect patients, if cognitive or motor deficiencies were existent within the ipsilesional space. Mattingley et al. (1994) showed direction hypokinesia and bradykinesia for severe neglect patients, when drawing a line to the contralesional side. This resulted in prolonged movement time, lower peak velocity and departures from optimal bell-shaped velocity profiles. The latter was measured through an increased time to reach peak velocity and an increased time from peak velocity to zero (Mattingley et al., 1994). According to Mattingley et al. (1994) the former parameter implies an increased *force production* to movements towards the contralesional side, i.e. patients spend most of the time in generating the forces, which are necessary to execute the movement. The latter parameter implies higher dependency on *visual guidance* because they also found slower response times for ipsilesional directed strokes (Mattingley et al., 1994). They argue that the decrease in execution time is due to the high proportion of decelerating (dependent on visual feedback) of neglect patients compared to a healthy control. Note that contrary to the work of Mattingley et al. (1994), this work does not focus on the intention of movement but on the characterization of motor and cognitive aspects within the ipsilesional space. An indirect parameter to measure automation is peak velocity. If peak velocity is abnormally small, it might not be possible to execute the movement properly, which can be a hint for motor or other cognitive deficits (Eichhorn et al., 1996). Derived from this, it might be true that the more severe the general execution deficiencies, the less automated the evaluated movement.

Rueckriegel et al. (2008) also found an association between speed and complexity of the task. The subject's personality has no influence, whereas verbal intelligence and motor training are possible moderating variables (Mergl, Tigges, Schröter, Möller & Hegerl, 1999). The results regarding gender and age are contradictory. While Rueckriegel et al. (2008) show a positive association between age, speed, and automation, the opposite effect was found by Mergl et al. (1999), where younger participants drew faster with a higher degree of automation. Similar contradictions were found regarding gender. Mergl et al. (1999) described no effect of gender, whereas Rueckriegel et al. (2008) measured higher velocities in male participants.

1.3 Development of novel tablet-based diagnostic tasks

Making use of the insights provided by previous research described in Section 1.1.5, novel computer-based tasks – which are specifically designed for the diagnosis of unilateral right-hemispheric neglect – are introduced. Apart from this application, these tasks can be extended to other neurological or neuropsychological diseases like idiopathic Parkinson's disease or dyspraxia. It consists of ten tasks, which can be subdivided into three categories: complex motor abilities, spatial orientation, and degree of automation. The categories with a description of the respective task are shown in table 1. Those tasks are based on well-known diagnostic procedures de-

Table 1

Categories of the tasks with a short description and information about the hand used to conduct these tasks in the scope of this study.

Category	Task	Hand
Complex motor abilities	Write the word *parallel*	Right
	Draw an Archimedes spiral	Both
Spatial orientation	Draw a horizontal line from right to left	Both
	Draw a horizontal line from left to right	Both
	Draw a square	Both
	Draw a circle	Both
	Draw a large circle	Both
	Draw a large rhombus	Both
Degree of automation	Draw large waves (like sine waves)	Both
	Draw large spikes	Both

scribed in section 1.1.3. Additionally, the Archimedes spirals have already been successfully used for the detection of essential tremor (Elble & Ellenbogen, 2017). The tasks are recorded by a graphical Wacom tablet, which can measure various parameters through the proprietary software CSWin (Mai & Marquardt, 2014). As shown in section 1.1.3, 1.1.4, and 1.1.5 the most important parameters to quantify the existence and in further consequence the severity of neglect are response time, pen pressure, peak velocity, peak acceleration, number of inversions in velocity, center of drawing on the x-axis, height of drawing and ratio of pen up and down time. While response time is a meaningful predictor for the severity and existence of neglect, Schendel and Robertson (2002) recommend velocity and acceleration instead. This decision is based on the fact that the latter can be measured every few milliseconds, which increases precision. Velocity and acceleration should also be meaningful predictors, since they are a function of response time. The focus of this study is the acceleration and velocity profile as well as the number of inversion in velocity to assess the degree of movement automation. Peak velocity and peak acceleration are investigated additionally, since meaningful reductions within those parameters might indicate deficiencies in movement execution (see section 1.2). Reference values are provided in appendix A.3. These tasks might be applied to various diseases with a wide range of symptoms, but have to be evaluated on healthy participants first. The following step would be the application on neglect patients.

1.4 The role of visual feedback in hand-writing and drawing

The computer-based diagnostic tasks described in section 1.3 are implemented on a graphical tablet without visual feedback. There are some relevant commonalities and differences between writing with or without feedback. According to Olive and Piolat (2002) quality is not affected, although the subjects need more time to draw without visual feedback. Furthermore, the size of hand-writing is meaningfully larger (Potgieser, Roosma, Beudel & de Jong, 2015). Hepp-Reymond, Chakarov, Schulte-Mönting, Huethe and Kristeva (2009) state that there is a higher level of automation without visual feedback. When writing the word *parallel* an increased number of pen touches and inversions in velocity as well as a decrease of mean stroke frequency are observable (Hepp-Reymond et al., 2009). There are no differences in age regarding the influence on letter size, velocity, and readability in missing visual feedback (Guilbert, Alamargot & Morin, 2019). Note that the graphical tablet device used for this study does actually have a slight visual feedback caused by the natural wear of the pen tip on the tablet's surface.

1.5 Hypotheses

The hypotheses are tested on healthy participants exclusively in order to build a basis for following clinical investigations. All evaluated tasks are conducted solely with the right (dominant) hand. This study focuses on the degree of automation measured through velocity and acceleration profiles, and number of inversions in velocity (NIV), which are recorded by the computer-based tablet program. Peak velocity and peak acceleration are investigated additionally, since they could have an indirect influence on movement execution in general (e.g. peak velocity being too low to execute a given task properly). More specifically, the expectations at hand can be divided into four aspects:

The velocity profile of every person should be normally distributed and thus bell shaped. The wave drawing task will be evaluated for this hypothesis. For neglect patients, a skewed distribution would be expected.

The same applies to the acceleration profile, holding the additional expectation of a distribution mean around zero. In this case, the wave drawing test will be used again.

It is expected that the dependent variables peak velocity, peak acceleration, and numbers of inversions in velocity are influenced by the duration of education and frequency of writing but not by gender and age when conducting a task of wave drawing. Potential confounding variables are important to identify before conducting clinical trials with neglect patients.

When drawing horizontal lines, the peak velocity is expected to differ between line direction but neither between age groups nor gender. For right-hemisperic neglect patients, the peak velocity is expected to decrease, especially for leftward line drawing compared to a healthy control.

2 Methods

2.1 Study design

The participant is informed about the study's purpose and has to confirm the declaration of consent (see appendix A.5). Demographic variables like age, gender, years of education, visited school types, and the current job are collected. For participation, several restrictions were made. The participants have to be at least 70% right-handed, which is measured by the modified list for hand preference, quantifying the dominant hand through the sum of ten dichotomous items (Salmaso & Longoni, 1985). No history of neurological or psychiatric diseases, no repeated operations with general anesthesia or other severe limitations of cognition are allowed to be declared and they have had to undergo at least eight years of some kind of scholastic or academic education. The frequency of hand writing is measured on a nominal scale (rather less, rather more). The study itself contains 23 writing or drawing tasks with the right, dominant hand and 19 tasks with the left hand. Eleven of those 23 tasks are called standard writing evaluation and are introduced in the CSWin manual (Mai & Marquardt, 2014). The other 10 tasks represent the novel assessment with specialized tasks for the diagnosis of neglect patients as described in section 1.3. The four remaining tasks only conducted with the right hand are those in which a word or a sentence has to be written either on paper or tablet. The procedure follows a strict manual (see appendix A.4), as the task execution might vary elsewise to a certain degree caused by different interpretation of the task at hand.

First, the subject has to conduct two Pen-and-paper tests with the right hand: write the German sentence *Die Wellen schlagen hoch* (engl. The waves wave high) at normal speed and follow the line in a template of the Archimedes spiral as accurately and fast as possible (see appendix A.6). After that, the standard writing evaluation is conducted with the right hand on a graphical tablet. The subject has to write the German sentence *Die Wellen schlagen hoch* and then draw two of the small letter L in cursive writing repeatedly until the time or the space on the tablet runs out. After that, one has to write up and down strokes repeatedly with a movement from the wrist in normal speed and faster. Afterwards the same gets repeated with a fixed wrist providing that the pen up and down strokes are executed through finger motion exclusively. Then curly lines should be drawn which are to look like the large Letter O. Again, this task is performed once in normal speed and once faster.

In addition, the curly lines have to be drawn with less pressure and with closed eyes. The eleventh and last task consists of meaningless scribbling. Subsequently to the standard writing evaluation, the tasks of the novel assessment for neglect patients are conducted as described in section 1.3. Afterwards both have to be done with the left hand, but the pen-and-paper tasks and those involving the subject to write a word or a sentence are left out. In total, the study requires about 15 to 20 minutes. Velocity and acceleration are measured every 5ms and peak velocity, peak acceleration, and NIV are calculated by the program CSWin.

The data is collected on a laptop with Windows 10 (1803) with CSWin version 2016 release 18.061. The filter bandwidths within CSWin are 30ms, 50ms for the first derivation, and 70ms for the second derivation. The recordings use kernel smoothing as described by Marquardt and Mai (1994) and Mai and Marquardt (2014). The hardware in use is a Wacom Intuos Pro graphical tablet (size M) with a Wacom pro pen 2. The choice of pen is important as the measured pressure may vary across different pens. All physical buttons (of the tablet and the pen) are disabled. The Wacom driver's version is 6.3.35-3 with a resolution of 5080dpi and a data rate of around 200Hz.

2.2 Data analysis

All descriptive and inferential statistical analyses are conducted in R 4.0.2 (R Core Team, 2020). In the sense of reproducibility, the R script and data sets are available online (https://github.com/j3ypi/Masterthesis). Let the error of the first kind α be denoted as 5%. All analyses are solely based on tasks performed with the right hand. Descriptive statistics in the form of range, mean, and standard deviation are calculated for the demographic variables age and years of education. To show the observed distribution of age, a histogram is drawn additionally. Frequencies are provided for the categorical variables gender and frequency of writing. Range, quartiles, median, mean, and standard error are calculated for the dependent variables peak velocity, peak acceleration, and NIV for the wave drawing task. The degree of automation is measured for the wave drawing (task number 15) through velocity and acceleration profiles for each person at every time of measurement. Additionally, NIV provides an indication for automation. Furthermore, peak velocity and peak acceleration are evaluated. For the horizontal line drawing tasks (task number 13 and 14) peak velocity is calculated.

To gain information about whether the velocity and acceleration profile are normally distributed, Shapiro-Wilk tests are performed for every person individually. To investigate the influence of years of education, gender, age, and frequency of writing (predictors) on peak velocity, peak acceleration, and NIV (dependent variables) a multivariate ordinary least squares linear regression is used. To check the hypothesis of possible differences regarding the peak velocity (dependent variable) in respect of age groups, gender (between-subject), and line direction (within-subject), when drawing a long horizontal line leftwards and rightwards, a repeated measures ANOVA is used. The effect size is reported in form of a generalized η^2, because it provides valid comparison between studies with between and within subject designs in contrast to the usually used partial η^2 (Bakeman, 2005). To check the assumptions of a normal distribution of the residuals when calculating the linear regression models, Q-Q Plots are used. Quantile plots are also drawn for the dependent variable peak velocity before conducting the repeated measures ANOVA, since normality is a necessary assumption.

2.3 Sample size calculation

Sample size calculations are conducted with g*power (Faul, Erdfelder, Lang & Buchner, 2007). The least powered statistical method used in this study is the repeated measures ANOVA. Thus, sample size calculations are done for the F tests executed in those ANOVAs. Given three groups of different age, an α-level of 5%, a statistical power of at least 95%, an expected effect size f of 0.3, and two-time measurements for each person, a total sample size of 51 is required. Note that the expected effect size can be chosen rather large since the practical consequences of overlooking an effect is acceptable in this case in respect of an economical viewpoint. This is due to the fact that healthy participants are investigated, where false positive results have no serious consequences.

2.4 Sample description

The sample of 51 persons is pseudo-random as several familiar persons were recruited as participants. The subjects are divided by age in three subgroups with 17 persons per group (18 to 29 years, 30 to 49 years, older than 49 years). The average

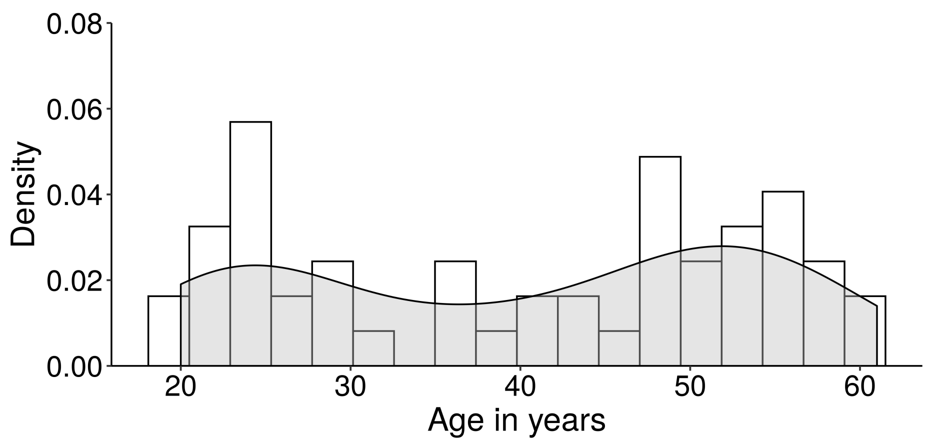

Figure 1. Histogram and probability density function for the distribution of age.

age is 40.16 (*SD* = 13.69) ranging from 20 to 61. As illustrated by the distribution of age in figure 1, age is not uniformly distributed, as there are less persons between 30 and 40. 23 males and 28 females were tested. 20 persons have declared to do rather less handwriting compared to 31 who declared to write much. The minimum years of education are 9 years and the maximum 21 years with 16.04 (*SD* = 2.47) on average. According to the EHI Test of hand preference two subjects are 70% right-handed, two 80%, and two 90%, while the rest indicates to be 100% right-handed.

3 Results

3.1 Wave drawing

The descriptive statistics of the dependent variables for the wave drawing task are shown in table 2. Note that peak velocity and peak acceleration are calculated by the program CSWin. The differences between those and the maximum of all velocity and acceleration measurements is probably caused by CSWin, where extreme observations might be excluded by default.

Table 2

Descriptive statistics for the dependent variables velocity [$\frac{mm}{s}$], acceleration [$\frac{mm}{s^2}$], NIV, peak velocity [$\frac{mm}{s}$], and peak acceleration [$\frac{mm}{s^2}$] for the wave drawing task.

Variable	N	Min	$Q_{25\%}$[1]	Mean	Median	$Q_{75\%}$[1]	Max	SE[2]
Velocity	36,814	8.3	196	309	282	398	1,771	0.82
Acceleration	36,814	-178,986	-1,950	-197	0	1,980	73,000	33
NIV	51	1.0	1.0	1.6	1.3	1.73	9.7	0.18
Peak Velocity	51	231	416	548	541	650	1,359	3.66
Peak Acceleration	51	1,058	4,430	9,555	8,546	12,887	26,081	120

[1] 25% and 75% quartiles [2] Standard error (SE)

Velocity profile. As displayed in appendix A.1, all conducted Shapiro-Wilk tests are significant, which indicates a violation of the assumption of an underlying normal distribution. Note that the sample size (here measurement time points) is rather large. Hence, the power of the Shapiro-Wilk test is high, which might lead to the detection of small and potentially negligible violations of the normal distribution. Figure 2 (a) shows the overall probability density function of velocity, where it is evident that the overall velocity distribution looks skewed to the left with a long right tail. A possible reason for the significant test statistics gets apparent after looking at individual velocity profiles (see table 5 in appendix A.1). An example is shown in figure 2 (c) as a

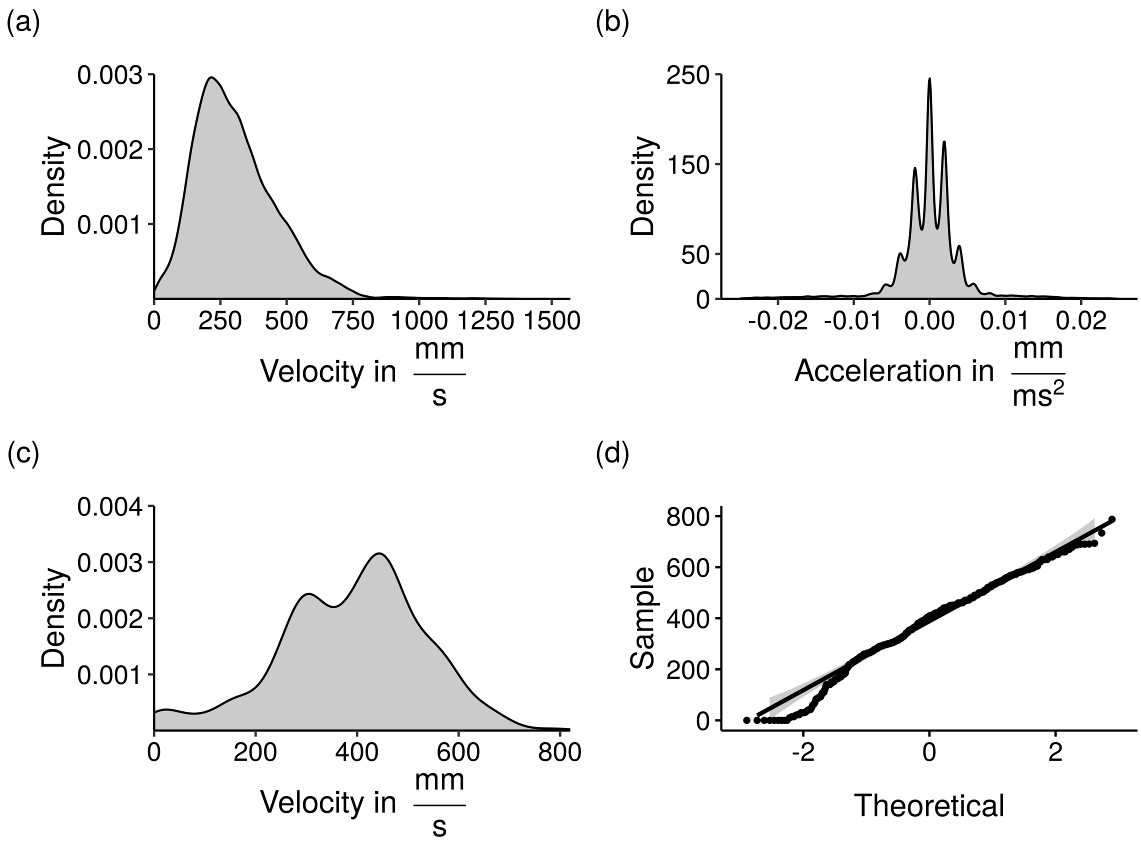

Figure 2. (a-b) Probability density functions for the task of drawing waves for all persons (a) of velocity in $\frac{mm}{s}$ and (b) of acceleration in $\frac{mm}{ms^2}$. (c-d) Velocity profile of one model person shown as (c) density function and (d) Q-Q plot. Note that only tasks with the right hand are evaluated.

density function of a single subject. Apparently, the measured velocity is not normally distributed, instead its distribution is bimodal having two local maxima. For further inference, figure 2 (d) displays the Q-Q plot for the exact same velocity values from the person displayed in (c). The Q-Q plot suggests no strong violation of the normal distribution. Even though the Q-Q plot indicates that the null hypothesis might be acceptable, the test statistics and velocity profiles suggest otherwise.

Acceleration profile. The same holds true for the individual acceleration profile as shown in table 5 in appendix A.1. While the estimates W_a actually do vary slightly, all *p*-values of the Shapiro-Wilks tests are smaller than .001. Figure 2 (b) provides insights into the acceleration profile over all subjects. Note that the most extreme values (peak acceleration more than $\pm$ 25 000 [$\frac{mm}{s^2}$]) are removed for illustrative purposes. While the acceleration values are distributed symmetrically around 0, it is not bell-shaped having at least five notable local maxima. This supports the results from table 5 in appendix A.1, where each person's profile deviates from a Gaussian distribution.

Table 3

Results of the multivariate linear regression model for the dependent variables peak velocity, peak acceleration, and NIV with β-coefficients, standard errors (SE), t-values, and p-values.

Dependent variable	Term	β	SE	t	p
Velocity [$\frac{mm}{s}$]	Intercept	781.48	210.45	3.71	0.001
	Years of education	-12.97	11.77	-1.10	0.276
	Gender	-28.96	59.92	-0.48	0.631
	Age	-0.59	2.02	-0.29	0.770
	Frequency	23.25	58.43	0.40	0.692
Acceleration [$\frac{mm}{s^2}$]	Intercept	13,490.11	6,630.96	2.03	0.048
	Years of education	-467.56	370.90	-1.26	0.214
	Gender	-2,704.03	1,887.91	-1.43	0.159
	Age	99.60	63.48	1.57	0.124
	Frequency	1,726.89	1,840.96	0.94	0.353
NIV	Intercept	2.49	1.39	1.79	0.079
	Years of education	-0.06	0.08	-0.71	0.481
	Gender	-0.44	0.40	-1.11	0.275
	Age	0.01	0.01	0.95	0.348
	Frequency	-0.44	0.39	-1.13	0.263

Peak velocity, peak acceleration, and NIV. The residuals of all regressions are approximately normally distributed (see figure 4 in appendix A.2). As displayed in table

3, none of the conducted Wald tests show significant influences of years of education, gender, writing frequency or age on the dependent variables peak velocity, peak acceleration or NIV. Note that the cause of the increased standard errors of gender and writing frequency is due to the fact that binary variables typically contain less information. The regression model with peak velocity as regressand and years of education, gender, writing frequency and age as predictors, has an adjusted R^2 of $-.050$. The global F test results in $F(5, 46) = 0.40$, $p = .807$, indicating that there is no notable explanation of the variance of velocity through the demographic regressors. This suggests that none of the β-coefficients within the models differ from zero. The statistical test results are similar for peak acceleration and NIV. For the former, the adjusted R^2 equals to .035 with a global hypothesis test holding $F(5, 46) = 1.45$, $p = .233$. For the latter, the adjusted R^2 is .005 and the global F test results in $F(5, 46) = 1.07$, $p = .383$. In conclusion, none of the regressors have any notable association with peak velocity, peak acceleration, and the number of inversions in velocity.

3.2 Line direction

Descriptive statistics of the peak velocity for leftward and rightward horizontal line drawing are illustrated in table 4. Peak velocity is very likely decreased in patients

Table 4

Descriptive statistics for the dependent variable peak velocity $[\frac{\text{mm}}{\text{s}}]$ *for the horizontal line drawing tasks in both directions.*

Line direction	N	Min	$Q_{25\%}$[1]	Mean	Median	$Q_{75\%}$[1]	Max	SE[2]
Rightward	51	121	253	500	451	658	1,394	5.41
Leftward	51	90	223	356	308	456	1,069	3.67

[1] 25% and 75% quartiles [2] Standard error (SE)

with neglect and is related to drawing direction. It is analyzed for rightward and leftward horizontal line drawings on healthy participants. Hence, the data of the two-line drawing tasks are evaluated with an ANOVA, testing three independent hypotheses about differences for the between-subject factors age group and gender as well as for the within-subject factor line direction given a random variation within the persons. The age group shows no significant difference with $F(2, 47) = 2.44$, $p = .098$,

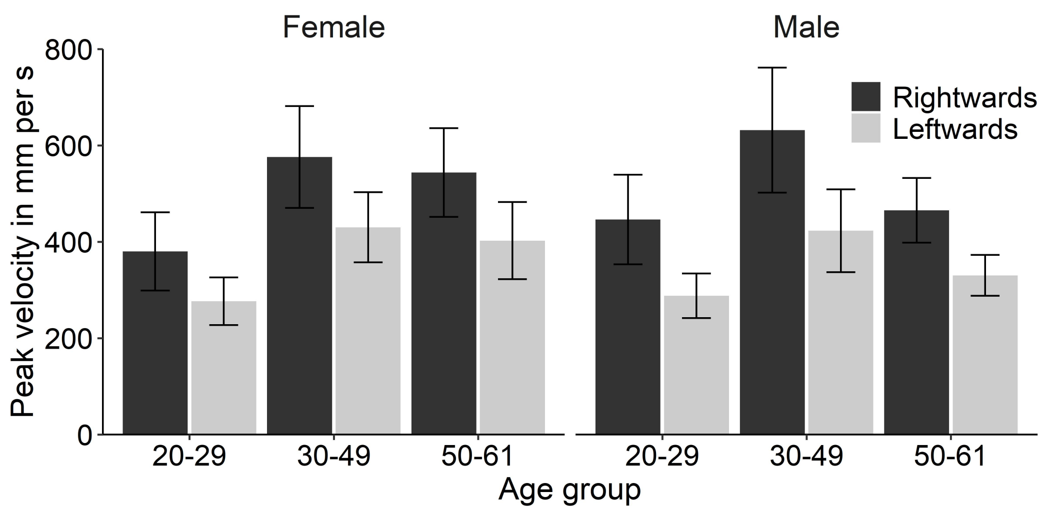

Figure 3. Barplot of the peak velocity $[\frac{mm}{s}]$ when drawing horizontal lines grouped by age, line direction (left to right, right to left), and gender with standard errors.

$\eta_g^2 = .09$. The same applies for gender, where the statistical test returns $F(1, 47) = 0.01$, $p = .942$, $\eta_g^2 < .01$, whereas a significant difference can be observed between the line direction with $F(1, 47) = 49.68$, $p < .001$, $\eta_g^2 = .10$. None of the interactions was significant. Note that the effect size adjusted for within subject designs is still rather small. The group differences tested in the frame of this ANOVA are illustrated in figure 3, where it is shown that the velocity for rightward line drawing is higher with 500 $\frac{mm}{s}$ compared to 356 $\frac{mm}{s}$ for drawing from the right to the left.

4 Discussion

Conclusion. Since unilateral right-hemispheric neglect is one of the most prevalent diseases after a stroke, it is as important to measure its existence and severity as investigating the neuropsychological causes. There have been first attempts to digitize existing pen-and-paper test batteries in the context of diagnosing neglect (e.g. Guest & Fairhurst, 2002; Liang, Guest et al., 2010), which built the basis to create the novel tablet-based tasks introduced in the frame of this study. Evaluating the performance of healthy participants on those tasks represents a necessary step for future clinical use. As a requirement to make the diagnosis of neglect more precise, potential influencing factors have to be identified in healthy participants to control for confounding variables when comparing neglect patients with a healthy control group in further studies. The degree of automation is used to measure the cognitive condition, since it represents a suitable proxy for potential motor deficiencies even within the ipsilesional space (e.g. Eichhorn et al., 1996; Mai & Marquardt, 2014; Rueckriegel et al., 2008).

The assumption that the degree of automation – measured through velocity, acceleration, and number of inversion in velocity – is normally distributed, cannot be confirmed without restrictions. The statistical tests of each individual person show violations of the normal distribution, which are supported by the visualizations of the individual velocity distribution via density function but not via Q-Q plot. On the contrary, the velocity distribution over all persons seems to be more bell-shaped but with a left-sided skewness. This skewed distribution can be found consistently throughout literature for response times caused by few extreme values, which is typically resolved by taking the reciprocal value of the response time (Noorani & Carpenter, 2016). Since velocity is a function of response time, the reciprocal transformation could also be applicable in this context. The acceleration profile only shows symmetry but no Gaussian distribution. Note that the unit of acceleration is different in figure 2 (b) to the distribution of velocity for illustrative purposes. Hence, the displayed differences of less than ± 0.005 $[\frac{\text{mm}}{\text{ms}^2}]$ around the median of zero, which leads to the visible multiple local maxima, could be due to inaccuracies in measurement or kernel density estimation within CSWin. Another possible explanation for the violation of normality of velocity and acceleration could be the nature of statistical tests of normality. Although the Shapiro-Wilk test is not as sensitive to violations of the normal distribution as the Kolgomorov-Smirnov test, the amount of measured time points every five milliseconds ranging from 380 to 1005 lead to a high power of the statistical tests, which in turn results in the detection of small deviations from the null-hypothesis. Thus, significant results of the Shapiro-Wilk tests should be interpreted with caution with the visualizations in the form of overall density and individual Q-Q plots in mind, which suggest more of an approximation to the Gaussian distribution and are hence more coherent with literature (e.g. Eichhorn et al., 1996; Mai & Marquardt, 2014; Rueckriegel et al., 2008; Schoemaker et al., 2005). More precisely, the normal distribution hypothesized by literature in healthy participants might be approximated well enough as Q-Q plots show.

Another indicator for a normal distribution is the NIV parameter. As table 2 illustrates, the NIV 25% quartile is still 1, which means that there is only one peak in velocity and hence an automated movement is observed. The differences between mean (1.6) and median (1.3) as well as the large maximum of 9.7 suggest some outliers. Since the median is still close to 1, one might rightfully assume an automated movement execution for most of the participants. This might serve as another hint for misleading Shapiro-Wilks test results (probably due to large sample sizes). The violations of normality in healthy participants have strong implications for clinical practice. On one hand, it suggests that classical hypothesis tests are too sensitive for violations compared to graphical verification (e.g. through Q-Q Plots). On the other hand, it has to be investigated to what extend the degree of automation (and hence the approximation to the Gauß distribution) decreases in neglect patients considering potential violations in healthy participants. If there are no meaningful differences in the ipsilesional space, it would strongly suggest that there are no motor or cognitive differences other than the shift in attention.

There is no association between the dependent variables peak velocity, peak acceleration, and the number of inversions in velocity and their regressors gender, age, years of education, and frequency of writing. The results regarding age have to be viewed with caution though. As shown in figure 1, age is not completely uniformly distributed. More importantly – as figure 3 suggests – the association between age and peak velocity does not appear to be linear. This might lead to misleading β-coefficients, i.e. while peak velocity increases from the young group to the middle, it then decreases significantly in the oldest group (at least for rightward lines). This is supported by the rather large F-value for gender, which would be considered significant at an α-level of 10%. This is especially interesting because response time of line horizontal line drawings is a common assessment to diagnose neglect. It needs to be further investigated, whether there are also differences in response time depending on line direction between neglect patients and a healthy control group. For further studies, a non-linear model might be more appropriate. The lack of differences regarding gender, supports the results reported by Mergl et al. (1999). Contrary to the results by Mergl et al. (1999) and Rueckriegel et al. (2008), no age differences were found. Mergl et al. (1999) found that younger participants drew faster with a higher degree of automation, while Rueckriegel et al. (2008) found the opposite (older participants drew faster with a higher movement automation). The observations of this study contradict either results. The results of the repeated measures ANOVA suggest an influence of the task direction on the peak velocity, which is an important information when constructing tasks for neglect patients. If healthy participants differ in peak velocity too, the differences regarding line direction, which were previously found in neglect patients, might be artificial.

Limitations. There are certain limitations regarding the sample population as it is only pseudo-random containing familiar persons with a mean years of education of 16.04, which can be considered above average. The participants' age should be more uniformly distributed and contain more subjects between 60 and 90, as this is an important range for neuropsychological diseases like neglect. Retrospectively, the sample size calculations assumed an effect size which might have been too large, considering that the observed effects are rather small and thus hard to detect, requiring a larger power. This might be caused by general high variances between persons in motion execution. In addition, response times even differ notably within persons over repeated measurements (e.g. Noorani & Carpenter, 2016), which might hold true for velocity and acceleration as well. Thus, it implicates multilevel models as a more appropriate choice compared to models with pre-calculated data aggregations (e.g. peak velocity and acceleration). This is because multilevel models are able to account for intra-personal differences by modeling this variance with random effects (McElreath, 2020). Another limitation is the vaguely measured frequency of writing (rather less, rather much).

Final remarks. For future research, the tablet-based tasks as described in section 1.3 should be further refined. A piece of A4 paper should be added to the surface of the tablet, because it is not clear for the participant where to write or draw elsewise. There should not be a time limit, but instead another signal should be used to end the task such as lifting the pen from the tablet to a certain degree. As Liang, Guest et al. (2010) state, the most important measured parameters are, inter alia, the number of cancellations in the left down quadrant, the mean value of acceleration of the pen movement, the movement time in the bottom left quadrant, the height of drawing, and the ratio of pen-down to pen-up time. Hence, a cancellation task should be added. Those parameters and the degree of automation should be compared in a clinical trial in assessing differences between neglect patients and a healthy control group. Furthermore, the differences in diagnostic sensitivity and specificity between the *conventional* subtests of the Rivermead Behavioral Inattention Test and the novel tablet-based tasks should be compared. A focus of further studies should also be the replication of the findings towards potential confounding variables – especially age and gender. Furthermore, the intra-personal variance of velocity and its automation indicating profile in drawing and hand-writing tasks should be investigated. If the variance of the parameters varies across different measurement dates as much as response time (e.g. Noorani & Carpenter, 2016), this variation has to be accounted for. There are various attempts to model variation in response time like hierarchical

LATER (Linear Approach to Threshold Ergodic Rate), Drift Diffusion or Linear Ballistic Accumulation models (e.g. Mulder, Van Maanen & Forstmann, 2014; Ratcliff & McKoon, 2008; Roberts, Oravecz, Sprague & Geier, 2019). These models might be extended to this context, since velocity and acceleration are a function of response time. Thus, it introduces the possibility to model not just the specific outcome but every single measurement. Hence, not only aggregated dynamic measurements like mean or peak velocity are used for inference but every single measurement (e.g. every 5ms), minimizing the loss of information.

This study paves the way for clinical use, where it might potentially increase diagnostic sensitivity considerably. Standard values for comparisons in clinical settings are supplied by this work, which opens the possibility of first-time applications on unilateral right-hemispheric neglect patients independent of age, education, gender, and hand-writing frequency. This might lead to further insights about the origin of neglect and a more precise differentiation between motor and non-motor symptoms.

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A Appendix

A.1 Shapiro-Wilk test results

Table 5

Shapiro-Wilk test statistics for each person for peak velocity and peak acceleration with additional information about the amount of measured time points.

Subject ID	Time points	Velocity		Acceleration	
		Estimate W_v	p_v	Estimate W_a	p_a
1	784	0.99	< .001	0.70	< .001
2	650	0.99	< .001	0.88	< .001
3	783	0.98	< .001	0.73	< .001
4	728	0.99	< .001	0.63	< .001
5	619	0.99	< .001	0.79	< .001
6	759	0.98	< .001	0.69	< .001
7	639	0.94	< .001	0.89	< .001
8	887	0.96	< .001	0.73	< .001
9	768	0.96	< .001	0.52	< .001
10	756	0.96	< .001	0.92	< .001
11	808	0.97	< .001	0.83	< .001
12	733	0.97	< .001	0.43	< .001
13	493	0.97	< .001	0.87	< .001
14	775	0.99	< .001	0.92	< .001
15	467	0.97	< .001	0.76	< .001
16	848	0.99	< .001	0.69	< .001
17	773	0.97	< .001	0.95	< .001
18	815	0.98	< .001	0.66	< .001
19	622	0.97	< .001	0.37	< .001
20	700	0.99	< .001	0.80	< .001

21	573	0.98	< .001	0.76	< .001
22	686	0.97	< .001	0.86	< .001
23	985	0.98	< .001	0.83	< .001
24	995	0.95	< .001	0.69	< .001
25	709	0.95	< .001	0.69	< .001
26	877	0.97	< .001	0.74	< .001
27	1003	0.97	< .001	0.79	< .001
28	968	0.97	< .001	0.74	< .001
29	741	0.98	< .001	0.73	< .001
30	380	0.96	< .001	0.96	< .001
31	705	0.99	< .001	0.79	< .001
32	613	0.99	.022	0.75	< .001
33	423	0.97	< .001	0.93	< .001
34	705	0.94	< .001	0.50	< .001
35	795	0.96	< .001	0.84	< .001
36	708	0.99	< .001	0.80	< .001
37	648	0.97	< .001	0.93	< .001
38	698	0.99	< .001	0.89	< .001
39	446	0.97	< .001	0.95	< .001
40	671	0.99	< .001	0.76	< .001
41	999	0.96	< .001	0.73	< .001
42	786	0.94	< .001	0.75	< .001
43	716	0.97	< .001	0.78	< .001
44	715	0.98	< .001	0.94	< .001
45	835	0.96	< .001	0.78	< .001
46	1005	0.98	< .001	0.70	< .001
47	549	0.96	< .001	0.95	< .001
48	765	0.98	< .001	0.68	< .001

49	412	0.96	< .001	0.83	< .001
50	721	0.96	< .001	0.76	< .001
51	575	0.98	< .001	0.88	< .001

A.2 Q-Q plots of the residuals and peak velocity

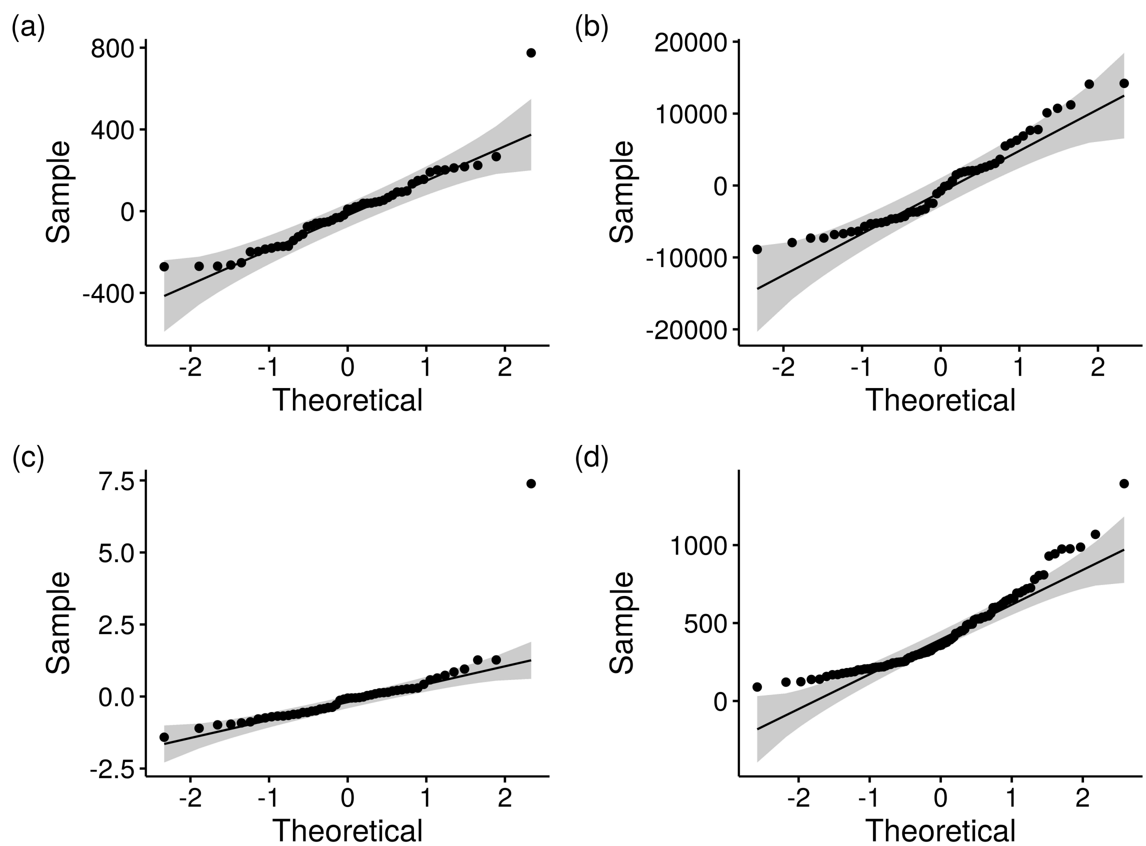


Figure 4. (a-c) Q-Q plots to check the assumption of normally distributed residuals for the regression analyses of (a) velocity, (b) acceleration, and (c) NIV. In (d) the normality of the peak velocity of all persons is examined by a Q-Q plot.

A.3 Reference values

Table 6

Reference values for the standard writing evaluation (task 1-11) and computer-based tasks (task 12-21) with frequency [Hz], writing force [N], NIV, and velocity [$\frac{mm}{s}$].

Task[1]	Frequency		Force		NIV			Velocity		% on
	μ	σ	μ	σ	μ^2	σ	$\%^3$	μ	σ	tablet
1	4.5	0.61	1.7	0.39	1.2	0.11	92.7	77.1	24.25	71.2
2	2.4	0.97	1.5	0.53	1.4	0.73	84.8	144.6	66.17	72.2
3	2.4	0.99	1.1	0.39	1.2	0.69	86.3	349.2	149.26	89.4
4	3.0	1.40	1.1	0.41	1.0	0.75	87.1	433.4	177.17	88.9
5	2.9	1.19	1.1	0.44	1.2	0.68	87.5	233.8	94.32	91.6
6	3.8	1.27	1.2	0.48	1.1	0.39	93.2	299.0	114.37	93.2
7	3.0	0.96	1.3	0.45	1.3	0.58	85.8	232.0	113.19	96.5
8	3.8	1.09	1.4	0.53	1.1	0.23	95.3	293.8	137.47	96.4
9	3.0	1.19	0.8	0.32	1.3	0.63	86.8	212.4	106.69	93.5
10	3.0	1.11	1.0	0.34	1.2	0.45	89.6	228.1	113.13	96.6
11	4.0	1.09	1.2	0.39	1.3	0.33	88.0	283.1	127.34	93.2
12	4.5	0.61	1.5	0.44	1.1	0.11	95.2	127.1	51.53	84.1
13	1.2	1.43	1.4	0.50	6.6	7.04	15.0	215.9	121.65	94.0
14	1.0	1.64	1.4	0.48	5.2	6.09	18.3	256.4	137.84	95.1
15	1.2	0.37	1.3	0.45	1.9	1.47	70.5	302.6	96.79	98.2
16	1.4	0.47	1.5	0.51	1.3	0.80	87.6	351.1	105.41	98.8
17	1.5	0.68	1.5	0.46	3.2	2.04	47.5	161.1	65.92	91.6
18	0.9	0.42	1.3	0.44	2.3	2.07	62.1	200.4	87.72	94.2
19	0.6	0.27	1.4	0.47	3.4	3.56	46.4	299.3	105.39	95.9
20	0.5	0.63	1.6	0.53	4.8	4.15	14.8	188.2	59.43	95.4
21	0.9	0.29	1.4	0.47	2.5	3.14	65.8	284.9	113.31	98.1

[1] **1:** Write *Die Wellen schlagen hoch*, **2:** Draw the small letter L in cursive writing repeatedly, **3:** Draw up and down strokes *from the wrist* in normal speed, **4:** The same as in 3 but faster, **5:** Draw up and down strokes with a fixated wrist in normal speed, **6:** The same as in 5 but faster, **7:** Draw curly lines like the letter O on top of each other in normal speed, **8:** The same as in 7 but faster, **9:** The same as in 7 but with less pressure, **10:** The same as in 7 but with closed eyes, **11:** Conduct meaningless scribbling, **12:** Write the word parallel, **13:** Draw a horizontal line from right to left, **14:** Draw a horizontal line form left to right, **15:** Draw large (sinus) waves, **16:** Draw large spikes, **17:** Draw a square, **18:** Draw a circle, **19:** Draw a large circle, **20:** Draw a large rhombus, **21:** Draw an Archimedes spiral

[2] Number of inversions in velocity: If NIV is larger than 1, there is more than one local maximum. The larger the value above 1, the less automated the movement.

[3] Percent of the segments within a task where NIV equals 1.

A.4 Instruction manual

Rechte Hand

Sie werden nun gebeten zwei Zeichenaufgaben an einem Blatt Papier zu absolvieren. Vor der jeweiligen Aufgabe, wird Ihnen eine Beschreibung vorgelesen. Ihre Zeit wird dabei gestoppt. Also starten Sie erst, wenn Sie mit *Beginnen Sie jetzt* darauf hingewiesen werden.

Bitte nehmen Sie jetzt den Kugelschreiber vor Ihnen in Ihre **rechte** Hand und setzten Sie sich so, dass Sie auf das Papier vor Ihnen schreiben können.

1. Test: Schreiben Sie den Satz *Die Wellen schlagen hoch* auf das Blatt Papier (DIN A4 quer) vor Ihnen. Ihre Zeit wird dabei gestoppt. Beginnen Sie jetzt.
2. Test: Zeichnen Sie die Archimedes Spirale in das Blatt Papier mit der Vorlage vor Ihnen nach. Ihre Zeit wird dabei gestoppt. Beginnen Sie jetzt.

Sie werden nun nacheinander 21 Schreib- und Zeichenaufgaben am graphischen Tablet vor Ihnen absolvieren. Sie werden nicht sehen, was Sie schreiben. Die Aufgaben sind dabei zeitlich unterschiedlich begrenzt. Bei normalen Schreibaufgaben soll in normaler flüssiger Handschrift geschrieben werden. Bitte beachten Sie, dass Sie nicht absichtlich schöner schreiben sollen, als sie es normaler Weise machen würden.

Bitte nehmen Sie jetzt den Stift in Ihre **rechte** Hand und setzen Sie sich so vor das graphische Tablet, dass Sie gut schreiben können.

1. Test: Schreiben Sie den Satz **Die Wellen schlagen hoch** auf das Tablet vor Ihnen.
2. Test: Schreiben Sie wiederholt jeweils zweimal den kleinen Buchstaben **L** in Schreibschrift [Beispiel zeigen].
3. Test: Schreiben Sie **Auf- und Abstriche** übereinander durch rasche alternierende Bewegungen im **Handgelenk**.
4. Test: Dies ist eine Wiederholung des vorgehenden Versuchs. Probieren Sie es nun etwas **flotter**. Dabei soll flüssig und flott geschrieben werden, aber nicht mit maximaler Geschwindigkeit.
5. Test: Schreiben Sie **Auf- und Abstriche** übereinander durch rasches Vor- und zurückfahren der **Finger**.
6. Test: Dies ist eine Wiederholung des vorhergehenden Versuchs. Probieren Sie es nun etwas **flotter**.
7. Test: Schreiben Sie mit schneller Schrift **Kringel** übereinander (etwa wie der Großbuchstabe O).
8. Test: Schreiben Sie Kringel erneut übereinander. Probieren Sie es nun etwas **flotter**.
9. Test: Schreiben Sie Kringel erneut übereinander. Probieren Sie es nun mit **weniger Druck**.

10. Test: Schreiben Sie Kringel erneut übereinander. Probieren Sie es nun mit **geschlossenen Augen**.
11. Test: Versuchen Sie schnelle sinnlose **Kritzel** auf der Stelle zu machen.
12. Test: Schreiben Sie das Wort **Parallel**.
13. Test: Zeichnen Sie einen langen Strich von **rechts nach links**.
14. Test: Zeichnen Sie erneut einen langen Strich aber dieses mal von **links nach rechts**.
15. Test: Zeichnen Sie **große Wellen** (Beispiel zeigen).
16. Test: Zeichnen Sie **zackige große Wellen**.
17. Test: Zeichnen Sie ein **Viereck**.
18. Test: Zeichnen Sie einen **Kreis**.
19. Test: Zeichnen Sie dieses mal einen **großen Kreis**.
20. Test: Zeichnen Sie eine **große Raute**.
21. Test: Zeichnen Sie die **Archimedes Spirale** (Beispiel zeigen).

Linke Hand

Nun werden wir den selben Test mit der linken Hand wiederholen. Nur das Schreiben des Satzes und des Wortes wird ausgelassen. Bitte nehmen Sie jetzt den Stift in Ihre **linke** Hand und setzen Sie sich so vor das graphische Tablet, dass Sie gut schreiben können.

1. Test: Schreiben Sie den Satz **Die Wellen schlagen hoch** auf das Tablet vor Ihnen.
2. Test: Schreiben Sie wiederholt jeweils zweimal den kleinen Buchstaben **L** in Schreibschrift [Beispiel zeigen].
3. Test: Schreiben Sie **Auf- und Abstriche** übereinander durch rasche alternierende Bewegungen im **Handgelenk**.

4. Test: Dies ist eine Wiederholung des vorgehenden Versuchs. Probieren Sie es nun etwas **flotter**. Dabei soll flüssig und flott geschrieben werden, aber nicht mit maximaler Geschwindigkeit.
5. Test: Schreiben Sie **Auf- und Abstriche** übereinander durch rasches Vor- und zurückfahren der **Finger**.
6. Test: Dies ist eine Wiederholung des vorhergehenden Versuchs. Probieren Sie es nun etwas **flotter**.
7. Test: Schreiben Sie mit schneller Schrift **Kringel** übereinander (etwa wie der Großbuchstabe O).
8. Test: Schreiben Sie Kringel erneut übereinander. Probieren Sie es nun etwas **flotter**.
9. Test: Schreiben Sie Kringel erneut übereinander. Probieren Sie es nun mit **weniger Druck**.
10. Test: Schreiben Sie Kringel erneut übereinander. Probieren Sie es nun mit **geschlossenen Augen**.
11. Test: Versuchen Sie schnelle sinnlose **Kritzel** auf der Stelle zu machen.
12. Test: Schreiben Sie das Wort **Parallel**.
13. Test: Zeichnen Sie einen langen Strich von **rechts nach links**.
14. Test: Zeichnen Sie erneut einen langen Strich aber dieses mal von **links nach rechts**.
15. Test: Zeichnen Sie **große Wellen** (Beispiel zeigen).
16. Test: Zeichnen Sie **zackige große Wellen**.
17. Test: Zeichnen Sie ein **Viereck**.
18. Test: Zeichnen Sie einen **Kreis**.
19. Test: Zeichnen Sie dieses mal einen **großen Kreis**.

20. Test: Zeichnen Sie eine **große Raute**.
21. Test: Zeichnen Sie die **Archimedes Spirale** (Beispiel zeigen).

A.5 Subject information and declaration of consent

Probandeninformation

Diese Studie dient dazu, Normwerte bei gesunden Probanden für verschiedene am Computer erfasste Schreibaufgaben zu erheben, um diese als Vergleichswerte für Patienten mit neuropsychologischen Erkrankungen (z.B. Neglect) zu verwenden. Die gesamte Untersuchung dauert etwa 25 Minuten und besteht aus zwei Teilen (Ausführung mit der rechten Hand und linken Hand). Die Untersuchung ist nicht invasiv und es bestehen keine Risiken für Sie.

Sie werden unterschiedliche Aufgaben durchführen. Die Aufgaben werden aus „Papier-und-Bleistift-Tests“ bestehen und aus Tests, die an einem graphischen Tablet erledigt werden. Ihre Teilnahme an diesen Untersuchungen erfolgt freiwillig. Sie können die Untersuchung ohne Angabe von Gründen jederzeit abbrechen. Die Ablehnung der Teilnahme oder ein vorzeitiges Ausscheiden aus dieser Studie hat keine nachteiligen Folgen für Sie.

Personenbezogene Daten dürfen im Rahmen dieser Studie nur mit ausdrücklicher Zustimmung des Betroffenen verwendet werden. Der Übermittlung der Daten im In- und Ausland erfolgt ausschließlich zu statistischen Zwecken und in anonymisierter Form. Allfällige Veröffentlichungen der Daten dieser Studie erfolgen ebenfalls in anonymisierter Form. Auch wenn Sie ohne Zwang und in Kenntnis der Sachlage für den konkreten Fall der Verwendung Ihrer personenbezogenen Daten im Rahmen dieser Studie zugestimmt haben, steht Ihnen die Möglichkeit offen, diese Zustimmung jederzeit ohne Angabe von Gründen und ohne nachteilige Folgen zu widerrufen. Dieser Widerruf bewirkt die Unzulässigkeit der weiteren Verwendung Ihrer personenbezogenen Daten, was im Regelfall mit Ihrem Ausscheiden aus der Studie verbunden sein wird.

Einverständniserklärung

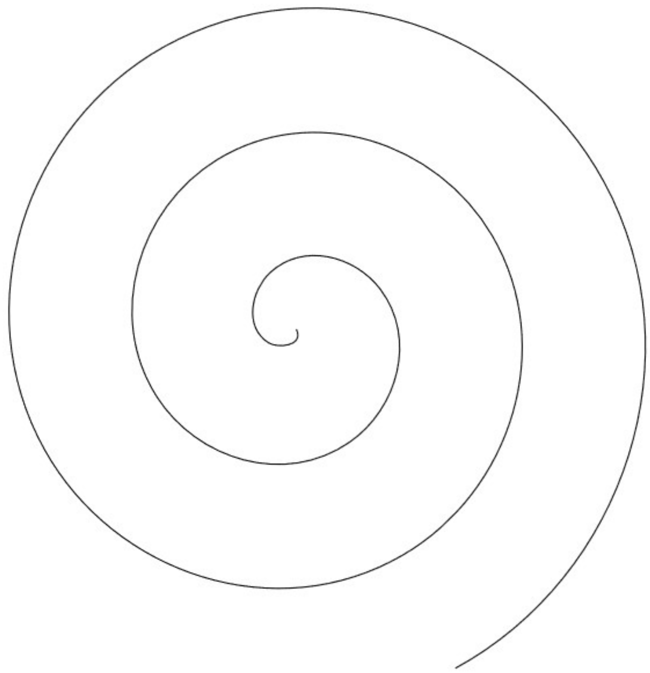
Ich bin mündlich und schriftlich über die Studie aufgeklärt worden. Ich habe die Probandeninformation und Einverständniserklärung gelesen und verstanden. Alle meine Fragen wurden beantwortet und ich habe derzeit keine weiteren Fragen mehr. Sollten sich während der Studie Fragen ergeben, kann ich mich jederzeit an den Untersucher wenden.

Mir ist bekannt, dass die Teilnahme an der Studie freiwillig ist und ich die Teilnahme jederzeit ohne Angabe von Gründen und ohne nachteilige Folgen widerrufen kann.

Nach der datenschutzrechtlichen Aufklärung erteile ich meine ausdrückliche Zustimmung, dass meine personenbezogenen Daten im Rahmen der oben genannten Studie zu dem eingangs angeführten Studienzweck verwendet werden dürfen.

Ich gebe hiermit freiwillig meine Zustimmung zur Teilnahme an der Studie. Eine Kopie dieser Teilnehmerinformation und Einverständniserklärung wird mir auf Wunsch ausgehändigt.

A.6 Archimedes spiral template



Eidesstattliche Erklärung:

Ich erkläre hiermit an Eides statt, dass ich die vorliegende Arbeit selbständig (mit Ausnahme der erklärten Teile), ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe. Die aus fremden Quellen wörtlich oder sinngemäß übernommenen Stellen und Gedanken sind als solche nach den Regeln der guten wissenschaftlichen Praxis kenntlich gemacht. Die Arbeit wurde bisher in gleicher oder ähnlicher Form keiner anderen Prüfungsbehörde vorgelegt.

. . . .

Datum Unterschrift

Declaration:

I confirm that this final thesis is my own work (except declared parts) and that I neither used any additional sources nor additional help, other than indicated. I declare that I correctly cited all sequences or ideas that have been taken from other sources according to the rules of good scientific practice. No part of this final thesis has been submitted at another university.

. . . .

Date Signature