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„Mixed Reality“ as a new rehabilitative approach to assist activities of daily living in patients with chronic neurological disease.

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“ (…) A picture is worth a thousand words.”
Patient with Alzheimer´s Dementia experiencing holographic cues.

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In 2008, as a newly qualified physiotherapist, I had my first contact with Apraxia patients and I will never forget how this clinical picture affected me: I wanted to understand the underlying mechanisms, but most of all I wanted to help. Unfortunately, I did not know how. I still love being a physical therapist, but traditional methods have obvious limitations. The fact that 10 years later my path has led me to research this topic and explore new treatment approaches, I consider to be an absolute privilege.

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Abbreviations

AADS – Apraxia and Action Disorganization Syndrome

AAL – Ambient Assisted Living

ADL – Activities of Daily Living

AR – Augmented Reality

AVG – Active Video Games

CG – Control Group

DILA-S – Diagnostic Instrument for Limb Apraxia-Short Version

DTx – Digital Therapeutics

MR – Mixed Reality

PTU – Pantomime of Tool Use

VR – Virtual Reality/Rehabilitation

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Abstract

Stroke and Alzheimer's dementia are among the leading causes of disability and need for long-term care in the elderly population and represent a growing global health challenge. There is an urgent need to make rehabilitation more efficient, promote independence and participation in daily life, and to ultimately reduce therapy and care costs. In particular, solutions that promote home-based therapies and reduce the burden on caregivers are needed. Besides a number of existing strategies, technological advances create new opportunities for patients with chronic motor and cognitive impairments. In this context, mixed reality (MR)-based therapy approaches, i.e., the use of virtual reality (VR), active video games (AVG), or augmented reality (AR), are considered as having great potential to contribute to the areas of both compensation and restoration. Given the growing evidence for the effectiveness of VR/AVG in stroke rehabilitation, it is important to better understand the factors that may distinguish particular systems or influence effectiveness in clients with different characteristics. In turn, knowledge about the impact of visual stimuli on corresponding motor programs and sensorimotor integration can contribute to the development of assistive systems.

The overall aim of this doctoral thesis was to contribute to the field of neurorehabilitation by exploring MR interventions as a possible approach to support activities of daily living (ADL) in patients with chronic neurological diseases. A total of four studies (studies I-IV) involving both patients with action disorders and healthy individuals was conducted to explore the impact of virtual environments and holographic stimuli on motor-cognitive performance. Affective mechanisms, i.e., engagement, enjoyment, motivation, immersion and presence, underlying motor learning in virtual environments after stroke were investigated using a scoping review method. In addition, AR technology (delivered via a head-mounted display/HMD) was used both as a unique method to unobtrusively support task performance in real-world environments and as a standardized research tool to investigate basic motor-cognitive mechanisms.

The results of the scoping review (study I) revealed a clear discrepancy between the theoretical importance of affective mechanism within VR/AVG interventions and actual measurement in stroke rehabilitation research. The growing emphasis on the role of affective factors in motor learning combined with these findings underline the need for standardized terminology and outcome measures to better understand and measure whether affective state differentiates VR/AVG use from traditional interventions and whether it contributes to intervention outcomes. Within a feasibility trial (study II) a multidimensional step-by-step guidance system was successfully implemented as an HMD-based assistive device and piloted in a real-world ADL task (making tea) in patients with Alzheimer's dementia and signs of apraxia. Overall acceptance was high, but patients needed significantly more time to complete the task and 30% of patients even failed the task when using the system. However, data analysis suggests that the applied support system may be of greater benefit to patients with more severe impairments. Most importantly, further research is needed to determine whether patients are actually able to integrate holographic stimuli into their activities and how these should be presented to influence performance and thus, compensate for motor-cognitive deficits. A randomized control trial (study III) shed some light into these questions by exploring whether the sensorimotor system responds to augmented environments in a way which reflects performance in the physical environment. By making use of the size-weight illusion phenomenon, the sensorimotor integration of holographic cues during a lifting task on real physical cubes was investigated in a group of healthy young subjects. Data suggests that holograms can manipulate perceptions during real object interactions. Initially, holographic cues may even dominate physical cues and cognitive knowledge, but are discarded when they conflict with cues from other senses. This was further supported by the results of a crossover trial (study IV) on post-stroke patients with apraxia and healthy control subjects, showing that the patients´ performance can be influenced when cued with visual stimuli of increasing saliency. Patients achieved significantly higher scores in a pantomime of tool use task with holographic or dynamic cues. When their performance was supported by dynamic holograms, it did not differ significantly from real tool demonstration, highlighting the potential of this type of cue.

In summary, MR was demonstrated to be a powerful tool to influence affective state and guide real-world interactions. It has been shown that holographic cues augmented in an everyday physical environment can attract attention and thus improve performance. However, the results also suggest that this may lead to distraction from real-world activities, as perception of and response to virtual cues is influenced by a number of factors, including personal conditions, hardware-related features, design principles, the environment, and user affect. These findings make an important contribution to the development of HMD-based holographic cueing systems, intended to enable people with action disorders to lead a self-determined life at home.

Zusammenfassung

Schlaganfall und Alzheimer Demenz gehören zu den häufigsten Ursachen für Behinderungen und Pflegebedürftigkeit in der älteren Bevölkerung und stellen eine wachsende globale Gesundheitsherausforderung dar. Es besteht dringender Bedarf, die Rehabilitation effizienter zu gestalten, die Selbstständigkeit und Teilhabe am täglichen Leben zu fördern sowie Therapie- und Pflegekosten zu senken. Es werden insbesondere Lösungen benötigt, die häusliche Therapien fördern und die Belastung des Pflegepersonals verringern. Neben einer Reihe bestehender Strategien schafft der technologische Fortschritt neue Möglichkeiten für Patienten mit chronisch motorischer und kognitiver Beeinträchtigung. In diesem Zusammenhang wird Mixed-Reality (MR)-basierten Therapieansätzen, d.h. dem Einsatz von virtueller Realität (VR), aktiver Videospiele (AVG) oder erweiterter Realität (Augmented Reality/AR), großes Potenzial zugeschrieben, um sowohl die Kompensation als auch die Wiederherstellung beeinträchtigter Funktionen zu unterstützen. Angesichts wachsender Evidenz zur Wirksamkeit von VR/AVG in der Schlaganfallrehabilitation ist es wichtig, jene Faktoren besser zu verstehen, die spezifische Systeme unterscheiden oder die Wirksamkeit bei Patienten mit unterschiedlichen Merkmalen beeinflussen können. Darüber hinaus kann das Wissen über die Auswirkungen visueller Stimuli auf die entsprechenden motorischen Programme und der sensomotorischen Integration zur Entwicklung von Assistenzsystemen beitragen.

Das Ziel dieser Doktorarbeit war es, einen Beitrag auf dem Gebiet der Neurorehabilitation zu leisten, indem MR-Interventionen zur Unterstützung von Aktivitäten des täglichen Lebens (ADL) bei Patienten mit chronisch neurologischer Erkrankung untersucht wurden. Anhand von vier Studien (Studien I-IV), an denen sowohl neurologisch betroffene Patienten mit Handlungsstörungen als auch gesunde Personen teilnahmen, wurde der Einfluss virtueller Umgebungen und holografischer Stimuli auf die motorisch-kognitive Leistungsfähigkeit untersucht. Affektive Mechanismen, d.h. Engagement, Vergnügen, Motivation, Immersion und Präsenz, die mit motorischem Lernen in virtuellen Umgebungen nach einem Schlaganfall in Zusammenhang gebracht werden, wurden mittels Scoping Review Methode untersucht. Zudem wurde AR-Technologie (unter Verwendung eines Head-Mounted Display/HMD) sowohl als einzigartige Methode zur Unterstützung von Aufgaben in realer Umgebung, als auch als standardisiertes Forschungsinstrument eingesetzt.

Die Ergebnisse des Scoping Reviews (Studie I) zeigten eine deutliche Diskrepanz zwischen der theoretischen Bedeutung affektiver Mechanismen bei VR/AVG-Interventionen und der tatsächlichen Erfassung innerhalb der Schlaganfall-Rehabilitationsforschung. Die zunehmende Bedeutung der Rolle affektiver Faktoren beim motorischen Lernen in Verbindung mit diesen Erkenntnissen unterstreicht die Notwendigkeit standardisierter Terminologie und Ergebnismessung, um besser zu verstehen und zu bewerten, ob der affektive Zustand die VR/AVG-Nutzung von traditionellen Interventionen unterscheidet und zu den Behandlungsergebnissen beiträgt. Im Rahmen einer Machbarkeitsstudie (Studie II) wurde eine multidimensionale Schritt-für-Schritt-Anleitung erfolgreich als HMD-basiertes Assistenzsystem implementiert und anhand einer realen ADL-Aufgabe (Tee kochen) bei Patienten mit Alzheimer Demenz und Anzeichen von Apraxie erprobt. Insgesamt war die Akzeptanz hoch, allerdings benötigten die Patienten unter Verwendung des Systems deutlich mehr Zeit zur Durchführung und 30% der Patienten scheiterten an der Aufgabe. Die Datenanalyse deutet jedoch darauf hin, dass das verwendete Unterstützungssystem für Patienten mit schwereren Beeinträchtigungen von größerem Nutzen sein könnte. Vor allem aber bedarf es weitere Forschungsinitiativen, um herauszufinden, ob Patienten überhaupt fähig sind, holografische Stimuli in ihre Aktivitäten zu integrieren und wie diese präsentiert werden sollten, um die Leistung zu beeinflussen und somit motorisch-kognitive Defizite zu kompensieren. Eine randomisierte Kontrollstudie (Studie III) trägt zur Klärung dieser Fragen bei, ob etwa das sensomotorische System auf erweiterte Umgebungen in gleicher Weise reagiert wie auf physische Umgebungen. Unter Ausnutzung des Phänomens der Größen-Gewichts-Täuschung wurde die sensomotorische Integration von holografischen Hinweisen während einer Hebeaufgabe mit realen Würfeln bei einer Gruppe gesunder junger Probanden untersucht. Die Daten deuten darauf hin, dass Hologramme die Wahrnehmung während der Interaktion mit realen Objekten manipulieren können. Anfänglich können holografische Hinweise sogar physische Hinweise und kognitives Wissen dominieren, werden aber verworfen, sobald sie mit Hinweisen anderer Sinneseindrücke in Konflikt geraten. Diese Erkenntnisse werden durch die Ergebnisse einer Crossover-Studie (Studie IV) mit Patienten mit Apraxie nach Schlaganfall und gesunden Kontrollpersonen untermauert, in der gezeigt wurde, dass sich die Leistung durch visuelle Reize steigender Salienz beeinflussen lässt. Die Patienten erzielten bei einer Pantomime Aufgabe zur Werkzeugnutzung mit Hilfe holografischer oder dynamischer Reize signifikant bessere Ergebnisse. Bemerkenswerterweise unterschieden sich die Leistungen der Patienten nicht signifikant von der realen Werkzeugdemonstration wenn sie durch dynamische Hologramme unterstützt wurden, was das Potenzial dieser Art von Reiz unterstreicht.

MR stellt ein wirksames Instrument zur Beeinflussung des affektiven Zustands und zur Steuerung von Interaktionen in der realen Welt dar. Holografische Hinweise, eingespielt in eine alltägliche physische Umgebung, können die Aufmerksamkeit lenken und somit die Leistung potentiell verbessern. Andererseits kann dies möglicherweise auch zur Ablenkung von realen Aktivitäten führen, da die Wahrnehmung von und die Reaktion auf virtuelle Hinweise von einer Reihe von Faktoren beeinflusst werden. Hierzu zählen sowohl personenbezogene als auch hardwarebezogene Merkmale, Designprinzipien, die Umgebungsform und der affektive Zustand des Nutzers. Die gewonnen Erkenntnisse leisten einen wichtigen Beitrag zur Entwicklung von HMD-basierten holographischen Cueing-Systemen, die es Menschen mit Handlungsstörungen ermöglichen sollen, ein selbstbestimmtes Leben zu Hause zu führen.

Chapter 1

General introduction

1. General introduction

Neurological disorders represent a growing global health challenge. Due to the increasing number of people with chronic neurological impairments and the associated long-term care (e.g., due to a history of stroke or Alzheimer´s Dementia/AD), there is a high demand for innovative rehabilitative approaches that promote restorative processes as well as compensatory strategies in daily life activities (Stinear et al., 2020). The use of Mixed Reality (MR) in Neurorehabilitation offers promising potentials for both, restorative training strategies (e.g., to deliver digital therapeutics/DTx) and compensatory approaches (e.g., applied as an assistive device) for patients with chronic neurological disorders. However, there are still a number of open questions that need to be investigated in order to make the available options even more effective and to approach the status of "standard of care". For instance, the evidence for virtual reality (VR) based interventions is steadily growing (Aminov et al., 2018; De Rooij et al., 2016; Doumas et al., 2021; Laver et al., 2017; Lohse et al., 2014; Staiano & Flynn, 2014). Little is known, however, how our affective state in virtual environments contributes to motor learning even though its purported affective impact has become a key marketing strategy for motor rehabilitation – will users achieve better training outcomes simply by the fact of being more motivated or having more fun during training? Moreover, since the development of stand-alone augmented reality (AR) based Head Mounted Displays (HMD), the use of AR-based guiding systems has gained great interest in the medical field and can become of particular relevance as a compensatory solution to support patients with cognitive decline in their activities of daily living (ADL). However, we do not know yet how holographic cues are integrated by our sensorimotor system – are we actually capable of perceiving and integrating holographic cues into our motor program? And if we are, which is the most efficient way in delivering holographic information to facilitate daily task performance in patients suffering from motor-cognitive impairments?

1.1 Thesis outline & objectives

The overall goal of this dissertation was to investigate MR interventions as a new rehabilitative approach to assist patients with chronic neurological disorders in their ADL. In particular, this thesis is devoted on understanding the fundamental role of affective factors in virtual environments for motor learning in the stroke population, as well as on the potential of overlaying holographic information onto the physical environment to assist patients with action disorders in their motor performance.

Within the **first chapter,** chronic neurological diseases are introduced, namely stroke and Dementia of the Alzheimer´s type. Further, related action disorders that are relevant for this thesis (paresis, apraxia) because of their impact on ADL are presented. This chapter also provides an overview of neurological principles in motor rehabilitation and existing cognitive rehabilitation approaches, including assistive technologies, followed by a section on MR with a focus on virtual rehabilitation and DTx.

Within the **second chapter** the central methods and materials of the studies that were published as part of this cumulative dissertation are presented. The first study deals with VR technology and AVG in the form of a scoping review. The other three studies are of experimental nature using AR technology, all designed to investigate the opportunities of holographic cueing and underlying cognitive mechanism.

The **third chapter** outlines the main results, i.e., a visual abstract, a summary, a statement on the author´s contributions using the Contributor Roles Taxonomy (CRediT) (Allen et al., 2019) and the original and full versions of the four articles that define this dissertation:

- Rohrbach, N., et al. (2019). What is the impact of user affect on motor learning in virtual environments after stroke? A scoping review. *Journal of neuroengineering and rehabilitation*, *16*(1), 1-14.
- Rohrbach, N., & Gulde, P., et al. (2019). An augmented reality approach for ADL support in Alzheimer's disease: a crossover trial. *Journal of neuroengineering and rehabilitation*, 16(1), 1-11.
- Rohrbach, N., et al. (2021). Fooling the size–weight illusion—Using augmented reality to eliminate the effect of size on perceptions of heaviness and sensorimotor prediction. *Virtual Reality*, 1-10.
- Rohrbach, N., et al. (2021). Improvement of apraxia with Augmented Reality: influencing pantomime of tool use via holographic cues. *Frontiers in neurology*, 1491.

Specifically, in chapter 3.1., the results of the conducted scoping review investigating affective mechanisms underlying motor learning in virtual environments after stroke are presented. By evaluating the available evidence, the aim was to examine the role of engagement, enjoyment, motivation, immersion and presence on motor learning in stroke rehabilitation and its relationships to each other.

Chapter 3.2 presents a feasibility study, as part of the Therapy Lens project, using an HMD-based AR application as a form of assistive technology by providing multidimensional step-by-step guidance. The goal was to evaluate holographic support during real tea making for patients with AD and signs of apraxia.

In chapter 3.3, AR technology was utilized as a unique research tool to understand the factors which drive the famous Size Weight Illusion (SWI) and in such, to examine if holograms are capable of manipulating perceptions in real object interactions. The goal was to investigate the impact of receiving holographic cues during a lifting task in a group of healthy young individuals. The results shed light into the question whether the sensorimotor system responds to augmented environments in a way which reflects performance in the physical environment.

In chapter 3.4, AR technology served again as a novel research tool, this time to study the underlying mechanism of apraxia. A combination of visual stimuli presented in different environments (i.e., screen vs. HMD) and different modes (i.e., static vs. dynamic) were provided in a pantomime of tool use (PTU) task and evaluated against each other in a group of post-stroke patients suffering from apraxia. The goal was to investigate the impact of visual cueing in apraxia and to identify the most beneficial way of augmenting feedback to the real environment.

The **fourth chapter** provides a discussion about the potential importance of affective state in learning and about the opportunities of virtual cueing and assistive technology is given, followed by an overall summary and outlook.

1.2 Chronic neurological diseases

The prevalence and incidence of neurological and neurodegenerative diseases will increase considerably in view of the increased life expectancy and is associated with high economic costs and a strong need for care for those affected (Erkkinen et al., 2018; Virani et al., 2020). Neurological diseases are diverse and often multifactorial with different causes affecting different brain regions, requiring different therapeutic strategies (Rohrbach & Hermsdörfer, 2020). Within this thesis, the focus is laid on two major diseases of the central nervous system, namely *stroke* and *Dementia of the Alz-*

heimer`s type, because they account for the most common disorders of aging and frequently co-occur and influence each other (Zhou et al., 2015). Moreover, research on restorative strategies and compensatory solutions is of particular interest because both patient groups often suffer from long-term motor and cognitive impairments, which are seriously impacting the patient´s autonomy. For instance, a lesion in the central nervous system can lead to restrictions or even complete loss of mobility, making participation in social events, leisure activities or returning to work often impossible (Rohrbach & Hermsdörfer, 2020). Among a range of possible symptoms observed in patients' post-stroke or with AD, two common action disorders i.e., *paresis* and *apraxia,* are addressed within this dissertation because they are often persistent and known to have profound effects on quality of life.

1.2.1 Stroke

The aging population and accumulating risk factors lead to an increasing lifetime risk of stroke, with 17 million people globally being affected each year (Feigin et al., 2014). Stroke can be defined according criteria set by the WHO (World Health Organization) as "rapidly developing clinical signs of focal (at times global) disturbances of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of a vascular origin" (Aho et al., 1980). As such, a stroke is the consequence of sudden death of brain cells due to a lack of oxygen, in 87% caused by blockage of blood flow to the brain (ischemic stroke) or in 10% caused by rupture of a blood vessel (haemorrhagic stroke) (Johnson et al., 2016; Virani et al., 2020). With an 16.1% increase in the ischemic stroke prevalence rate from 2007 to 2017 and higher survival rates due to improved acute treatment, stroke remains a leading cause of chronic disability worldwide (Virani et al., 2020). The effects of a stroke vary and depend on the location and size of the lesion. Sensory, motor and cognitive impairments can make participation in social and community activities difficult and thus, severely impact a patient's quality of life (Kim et al., 2014; Mayo et al., 2002; Virani et al., 2020). For instance, action disorders post-stroke (e.g., paresis and apraxia) often limit stroke survivors in their basic daily life skills, such as locomotion or object manipulation (Sathian et al., 2011), or in fundamental complex activities, such as preparing a meal (refer to chapter 1.2.3 for details on action disorders). The global prevalence of 104.2 million stroke patients puts an associated burden on the healthcare system (Virani et al., 2020). In Germany only, the amount of stroke-related medical costs (including inpatient rehabilitation and follow-up care) is among the highest in the healthcare system, and can rise up to 43.000 Euro per patient (Düchs et al., 2012). In addition, the risk of developing secondary diseases increases significantly as a consequence of a stroke, which in turn leads to further health related problems. For instance, the risk of developing dementia (see 1.2.2), which is a major reason of functional dependency in the elderly, doubles due to stroke-related molecular and cellular changes (Vijayan & Reddy, 2016).

1.2.2 Dementia of the Alzheimer's type

Dementia represents the leading cause of disability and dependency among the elderly population. With over 10 million new cases each year, in 2020, a total of approximately 50 million people worldwide lives with some form of dementia. Due to demographic ageing, this number is believed to double every twenty years, reaching 82 million in 2030 and 152 million in 2050. Dementia is a collective term that refers to different brain disorders, leading to a fatal progressive decline in cognitive ability (ADI, 2021). Accounting for two-thirds of dementia patients aged over 65, dementia of the Alzheimer's type is the most common form. Having a stroke is a major factor for developing AD (Vijayan & Reddy, 2016). In turn, this neurodegenerative disorder, showing an accumulation of abnormal neuritic plaques and intracellular neurofibrillary tangles in the brain (Erkkinen et al., 2018; Kalaria, 2002), is associated with an increased risk of developing a stroke (Zhou et al., 2015). The clinical profiles of AD are heterogeneous and depend on the stage of the disease and affected brain areas. AD is characterized by an insidious onset and progressive impairment of behavioral and cognitive functions, including memory loss (e.g., impairment in learning and recall), problems with comprehension and language (e.g., word-finding deficits), visuospatial (e.g., spatial cognition-object agnosia, facial recognition issues) and executive dysfunction (e.g., impaired reasoning, judgment and problem solving). As a consequence of significant cognitive impairment and the presence of apraxia, patients have difficulties with complex ADL and familiar tasks, such as shopping, preparing meals and navigating routines and often lose their functional independence (ADIa, 2022; Erkkinen et al., 2018; Kalaria, 2002; Kumar et al., 2018). The expansion of the number of people suffering from dementia has momentous consequences for national care systems as well as a large economic impact, with annual global costs of US$ 1 trillion (ADI, 2021).

1.2.3 Action disorders and its impact on Activities of Daily Living

To accomplish everyday activities goal-directed actions are needed that are controlled by our sensorimotor system and driven by our motivational states (Frey et al., 2011). For instance, the successful preparation of a cup of tea requires the coordination of sub-movements (e.g., reaching for, grasping, and letting go of involved items) and the organization of multiple sub-goals which have to be sequenced in a logical order (e.g., the water has to be heated in a kettle first before being poured into a cup, and then, the correct ingredient has to be chosen out of a variety of options and inserted in the cup in an appropriate amount, and so on). Most stroke survivors or AD patients require some form of assistance in their daily live activities or are even fully dependent on caregivers due to action disorders. Paresis, which represents one of the greatest challenges after a stroke, and apraxia, a demanding motor-cognitive disorder that affects both, stroke survivors and people with AD, are described below.

Paresis

The most common motor disorder observed post-stroke and impairing function is paresis, the reduced ability to voluntary activate the spinal motor neurons, which is typically characterized by a complex collection of impairments, i.e., weakness, spasticity, a decreased ability to fractionate movements and higher-order planning deficits (Sathian et al., 2011). Approximately two-thirds of stroke patients suffer from long-term upper limb paresis and only a few show complete recovery at six months post-stroke (Kwakkel et al., 2003). As primarily a problem of movement execution, the underlying mechanisms of paresis is damage to the corticospinal system. Patients suffering from paresis may struggle in moving their upper or lower limbs; their movements appear slower and poorly timed, uncontrolled and uncoordinated, less precise and less efficient than usual, which is fundamentally impairing daily tasks and activities. The paretic syndrome can be accompanied by sensory and proprioceptive deficits or pain and is often associated with secondary complications (e.g., atrophy or contractures), which is additionally impairing the performance of everyday actions (Rohrbach & Hermsdörfer, 2020; Sathian et al., 2011).

Apraxia

Another common action disorder affecting both, patients after stroke and patients with AD, is the syndrome of apraxia and action disorganization (AADS) (Bieńkiewicz et al., 2014). Apraxia is typically defined referring to Rothi et al. (1997), as a "disorder of movement not caused by weakness, akinesia, deafferentation, abnormal tone or posture, movement disorders (such as tremors or chorea), intellectual deterioration, poor comprehension, or uncooperativeness" (Rothi & Heilman, 1997). Action disorganization syndrome describes the neuropsychological disorder after brain damage compromising the ability to sequence fixed chains of actions in an appropriate manner (Bieńkiewicz et al., 2014; Schwartz et al., 1991). AADS is a very heterogeneous, higher-order cognitive-motor disorder affecting complex, skilled movements, and a major predictor of poor ADL performance and of increased dependence on caregivers (Bieńkiewicz et al., 2014; Smania et al., 2006). Apraxia occurs after damage to various loci in a densely interconnected network of regions in the left temporal, parietal, and frontal lobes, observed in both ipsi- and contralesional limbs (Buxbaum & Randerath, 2018; Randerath, 2020) and often accompanied by comorbidity syndromes (e.g., aphasia) (Bieńkiewicz et al., 2014; Goldenberg, 2013). Typically, patients are impaired in using tools skillfully, pantomiming tool use actions, and recognizing or imitating other's gestures (Bieńkiewicz et al., 2014). Problems with recognition and imitation can make physical therapy interventions and communication more difficult (Buxbaum & Randerath, 2018; Randerath et al., 2017). Further, patients may struggle in carrying out multiple step actions, such as preparing a drink, because of being unable to select and sequence the appropriate motor programs or because of difficulties in integrating semantic and motor features of objects into their action plans (Finkel et al., 2018; Goldenberg, 2014). Consequently, patients often substitute inappropriate actions, mis-sequence actions or omit essential steps, impairing independent living and potentially even resulting in safety hazards in their home environment, such as not turning off the stove (Bieńkiewicz et al., 2014; Randerath et al., 2017). The reported prevalence rates for patients with right hemispheric stroke range between 0-34% (e.g., (Donkervoort et al., 2000)), between 28-57% for patients with left hemispheric stroke (e.g., (Bickerton et al., 2012; Donkervoort et al., 2000)) and between 32-69% in AD patients (e.g., (Ahmed et al., 2016; Ozkan et al., 2013)). Problematically, apraxia post-stroke is often persistent (Bickerton et al., 2012; Sathian et al., 2011), and difficulties in patients with AD increase with ongoing disease decline (with up to 98% of severely demented patients being affected) (Edwards et al., 1991).

1.3 Neurological Principles and Rehabilitation

As described in the preceding section, complex lesions of the central nervous system due to a stroke or AD often cause multiple disorders, thus, requiring a multi-factorial treatment approach, including pharmacological and rehabilitative interventions (Rohrbach & Hermsdörfer, 2020). Rehabilitation of motor impairments post-stroke is aiming to restore function (e.g., restitution of damaged tissue), reorganize intact neural pathways (e.g., substitution), and improve impaired motor skills in ADLs (e.g., compensation) (Dobkin, 2004; Kwakkel, 2006; Zeiler & Krakauer, 2013). Restitution hereby defines return to or towards premorbid levels of motor control and strength by directly working on the underlying mechanism (Pomeroy et al., 2011; Zeiler & Krakauer, 2013). In this regard, a large body of research is devoted on maximizing neuroplastic processes and to identify neurological principles that enhance motor learning and recovery (Kleim & Jones, 2008). Especially in chronic diseases, when symptoms become persistent or gradually progress with a high need for continuous support and care, compensatory approaches are more commonly applied, providing alternative strategies that make use of a patient´s residual effectors, muscles, or joints to accomplish the same task (Zeiler & Krakauer, 2013). Basic knowledge about these underlying processes is important for the choice of therapeutic interventions (e.g., restorative vs. compensatory strategies), and informs the design of new approaches that are aiming to make rehabilitation more effective. In such, this section introduces *neuroplasticity*, as the basis for functional restitution after acquired brain damage (Nudo et al., 1996), and several *active ingredients* of motor rehabilitation that appear to modulate specific brain areas or networks of brain regions. Further, a brief overview about traditional compensatory *cognitive strategies* for apraxia as well as on *assistive technologies* is given, aiming to reduce the effects of cognitive impairment on functions and abilities with a strong focus on ADL support.

1.3.1 Neuroplasticity and motor learning

A central goal in motor rehabilitation is to initiate motor learning in order to maximize neuroplasticity, i.e., the process of reorganization within the brain to recover from impairments (Kleim & Jones, 2008; Levin et al., 2015; Zeiler & Krakauer, 2013). Motor learning is hereby defined as a relatively permanent change in a motor skill, achieved through practice or experience, which can then be transferred to new learning situations (Schmidt & Lee, 2014). Even though recovery and adaptive plasticity can continue at any time after the event (Dobkin, 2004; Nudo, 2003), the first weeks after stroke seem to be of critical importance because most spontaneous biological recovery occurs (Dromerick et al., 2015; Zeiler & Krakauer, 2013). Spontaneous recovery occurs independently of interventions, however, there is growing evidence that neuroplastic changes following stroke can be influenced by learning and behavioral experience if the training follows certain criteria (e.g., by offering a sufficiently salient experience, with sufficient repetition and intensity (Kleim & Jones, 2008; Zeiler & Krakauer, 2013)). In this regard, a range of training interventions have been studied targeting motor rehabilitation post-stroke, including task-oriented training (Winstein et al., 2016), robot-assisted training (Rodgers et al., 2019), functional strength training (Pomeroy et al., 2018), active video gaming (Saposnik et al., 2016), virtual reality (Brunner et al., 2017), or constrained-induced movement therapy (Kwakkel et al., 2016). Specifying on the "active ingredients", i.e., the reasons why the intervention is expected to be effective (Whyte & Hart, 2003), and implementing them in clinical guidelines, is a major topic of neurorehabilitation research (Levac et al., 2012; Maier, Ballester, et al., 2019; Maier, Rubio Ballester, et al., 2019).

1.3.2 Active ingredients in post-stroke motor rehabilitation

Maier et al. (Maier, Ballester, et al., 2019) collected generally accepted principles of neurorehabilitation based on existing work on motor learning and recovery: massed practice/repetitive practice, spaced practice, dosage/duration, task-specific practice, task-oriented practice, variable practice, increasing difficulty, multisensory information, rhythmic cueing, explicit feedback/knowledge of results, implicit feedback/knowledge of performance, modulate effector selection, action observation/embodied practice, mental practice, and social interaction. Most knowledge is derived from the stroke population, however, because of showing similar cognitive, functional, and neuronal alterations, these principles are suggested to be applicable to other pathologies (such as AD (Kalaria, 2002)), too. Further, the important role of affective factors, such as motivation, enjoyment or engagement, by either indirectly (e.g., increased practice dosage) or directly (e.g., enhanced dopaminergic mechanism) influencing motor learning is an emerging field of research (Lohse et al., 2016; Winstein & Varghese, 2018; Wulf & Lewthwaite, 2016).

1.3.3 Cognitive rehabilitation following apraxia

As introduced in chapter 1.2, patients' post-stroke and with AD often share the presence of significant cognitive impairment and AADS. Buxbaum et al. (Buxbaum et al., 2008) identified several motor learning principles that may also be beneficial for the rehabilitation of apraxia, including distributed practice of the target task, contextual interference, feedback of results, and intensity of practice, with very little knowledge about how these principles are best parameterized (Buxbaum et al., 2008). Traditional cognitive rehabilitation approaches for apraxia revolve around physical and occupational therapy concentrating on compensatory approaches by providing external cues (Buxbaum et al., 2008; Cogollor et al., 2018; Goldenberg, 2013). Examples include strategy training (i.e., gradually teaching new ways to solve a task, including instructions, assistance, feedback) and verbalization (Geusgens et al., 2007; Goldenberg et al., 2001; Smania et al., 2006), errorless learning (i.e., the patient is guided through the correct sequence preventing errors to occur) (Goldenberg, 2013), and meaningful and task-specific training (Goldenberg et al., 2001). Further, practicing within the home environment was highlighted to play a major role, possibly because familiar situations could trigger ADL routines (Bieńkiewicz et al., 2014; Geusgens et al., 2007). Overall, the available evidence for cognitive rehabilitation in that field is insufficient to give clear recommendations for clinical practice (Gillespie et al., 2015) with limited generalization of apraxia training to untrained tasks (Bieńkiewicz et al., 2014). In this regard, first research activities on assistive technologies have been initiated aiming to provide ongoing ADL support in the patient´s home (Cogollor et al., 2018).

1.3.4 Assistive technologies

Advancements in wearable and sensing technologies resulted in a range of devices that have the potential to promote independency and autonomy for patients with chronic neurological disorders. For instance, telerehabilitation services for patients post-stroke (Laver et al., 2020) or with AD (Cotelli et al., 2019) have been implemented to provide rehabilitation for patients remotely using information communication technologies (ICT; such as videoconferencing, sensors or VR-programs). Ambient Assisted Living systems (AAL), have been developed aiming to assist people in their ADL at home by providing user-friendly products and services. AAL refers to technological solutions designed to support the elderly in their daily life in order to maintain independence and autonomy in a safe home environment for the individual by combining ICT and social environments, and in such, benefit the economy and society (Dohr et al., 2010). Today, already a range of assistive devices exist than can support patient´s mobility but also their memory, communication, safety, daily tasks, socialization activities, as well as independence and self-confidence, including automated reminders and prompts, medication aids, hearing and vision aids, locator devices, sensor and tracking systems, fall alarm systems, virtual assistants and robotic technologies, to only name a few (Alzheimer´s, 2019). For example, the CogWatch prototype provides a web based Personal Healthcare System for patients with AADS (CogWatch, 2021). CogWatch consists of a tablet computer, sensors attached to the objects, and a camera recording the activity. An integrated action-recognition system is aiming to prompt the correct action by giving visual, auditive, textual and haptic information (Pastorino et al., 2014). Another recent example in that field is the “digital cooking coach”. The smart kitchen system was designed for people with cognitive impairment providing projection-based visual feedback using Microsoft’s Kinect (V2) and auditory feedback via external speakers (Kosch et al., 2019). Even though assistive technologies and telerehabilitation platforms for motor and cognitive deficits represent an emerging and promising field, the evidence base is still limited and available systems need to be trialed beyond the proof-of-concept stage (Cogollor et al., 2018; Cotelli et al., 2019; Laver et al., 2020; Mantovani et al., 2020). Overall, MR-based guidance systems represent a growing area of research. Promising research in related sciences such as guided surgery or medical training shows the potential for applying the concept to neurorehabilitation. (Chen et al., 2017).

1.4 Mixed Reality Technology in Neurorehabilitation

The increasing number of people living with chronic neurological diseases creates a greater demand for rehabilitation services. For AD, there is currently neither proven effective prevention nor a cure available and its rehabilitation is complex due to its progressive nature (Erkkinen et al., 2018). Studies on the rehabilitation of apraxia are limited as compared to other domains and training approaches often do not generalize to untrained tasks, demonstrating the urgent need for effective rehabilitation strategies (Buxbaum et al., 2008; Buxbaum & Randerath, 2018; Cantagallo et al., 2012; Pomeroy et al., 2011; West et al., 2008). Regarding the motor rehabilitation post-stroke, promising research indicates that available interventions can be beneficial in regaining independence (Stinear et al., 2020). Still, to further promote the independence and participation in everyday life of those affected in the long term and also reduce therapy and care costs, interventions are needed that optimize acquisition, retention, and generalization of skills. Current findings from neuroscience can inform clinical practice. In such, novel rehabilitation techniques have been developed that are intended to specifically address neurorehabilitation principles, such as the mechanisms of functional neuroplasticity, including important elements like motor control and motor learning (see 1.3.1). Further, research is dedicated to finding solutions that provide home-based therapy and alleviate the burden on the caregivers. Indeed, the majority of adults aged 50 and older prefer to stay in their home environment as long as possible (Binette & Vasold, 2018), while over 50% of carers feel overwhelmed and affected in their own health as a result of their caring responsibilities (ADIa, 2022). Technological interventions, e.g., robotics and AAL systems (see 1.3.4) can incorporate these principles and needs. Further, the use of MR technology offers promising potential for both, restorative training strategies (e.g., using VR for motor learning) and compensatory approaches (e.g., using AR to guide daily activities). In addition, the development of digital therapeutics (see 1.4.3) is currently booming in the clinical field, aiming to prevent, manage, or treat a medical disorder or disease (DTA, 2019).

The upcoming sections present VR and AR as elements of the reality-virtuality continuum and define immersion and presence as important key concepts in MR environments, followed by an introduction into virtual rehabilitation as a promising form of digital therapeutics.

1.4.1 Reality-virtuality continuum

According to the reality-virtuality continuum (Figure 1), the real world (i.e., the physical environment) and the virtual world (i.e., a completely modelled environment) are laying on opposite sides of a spectrum (Milgram & Kishino, 1994). VR refers to a computer hardware and software system that generates interactive simulations of real or imagined environments with which participants engage using their own movements (Wilson et al., 1997) (see also Perez-Marcos (2018) for a discussion on VR terminology related to its field of application (Perez-Marcos, 2018)). In contrast to VR systems, in AR the user´s real environment is not replaced but rather enriched by spatially aligned virtual objects (Milgram & Kishino, 1994). Based on Azuma (1997), AR systems (1) should combine real and virtual objects in a real environment; (2) run interactively and in real time; and (3) register (align) real and virtual objects with one another (Azuma, 1997). Augmented reality and augmented virtuality (AV; where the augmentation is supplemented with real-time elements) operate in between the boundaries of the reality-virtuality spectrum and are part of what is known as mixed reality (Milgram & Kishino, 1994). MR environments differ by viewing medium (e.g., head mounted displays/HMD vs. screens), method of interaction (e.g., peripheral devices vs. motion sensor based recognition systems) and technological requirements (e.g., high end 3D multimodal platforms vs. simple gaming options) (Levin et al., 2015; Wilson et al., 1997). All these components are influencing the level of *immersion* and the sense of *presence*, which are known to be central key concepts within MR environments (Liberatore & Wagner, 2021).

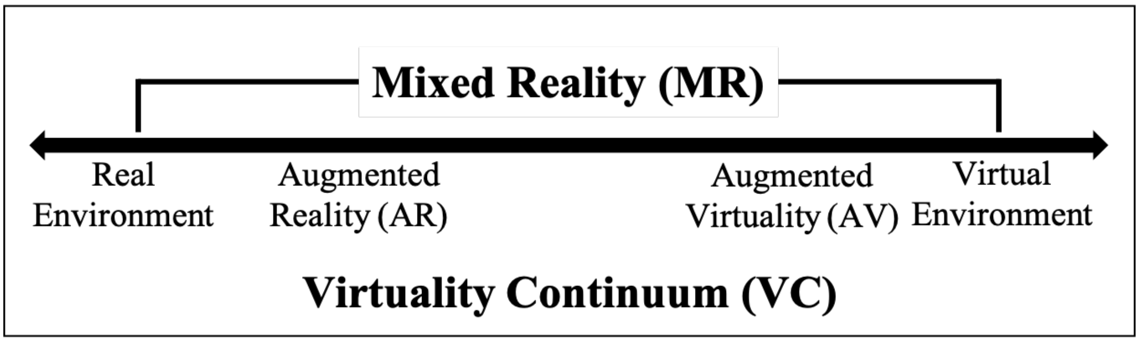


Figure 1. Simplified representation of the "virtuality continuum" according to Milgram & Kishino (1994).

Key concepts in Mixed Reality environments

Technological immersion refers to the level of physical stimulation applied to the sensory system and the sensitivity of the system to motor input. It can be defined as “the extent to which the VR system succeeds in delivering an environment which refocuses a user’s sensations from the real world to a virtual world” (Rose et al., 2018; Weiss et al., 2006). The degree of immersion is considered objective and measurable - one system can have a higher degree of immersion than another and depends on various technological factors, such as the rendering software, the quality of tracking, the provided realism, or the display technology of the system (e.g., the size of the field of view) and can be enhanced by adding other sensory cues (e.g., auditory or haptic) (Perez-Marcos, 2018; Sanchez-Vives & Slater, 2005; Slater, 1999, 2003). The psychological product of technological immersion is called presence (Bohil et al., 2011); the psychological feeling of “being there” instead of in the physical environment is influenced by many components, such as the characteristics of the user, the task, and the system (Sanchez-Vives & Slater, 2005; Weiss et al., 2006). AR stimulates a slightly different (Regenbrecht & Schubert, 2002) and higher sense of presence than VR due to the fact that the user can still see their own body interacting with real objects (Al-Issa et al., 2012). The degree of presence is often measured on the basis of self-reports and increasingly also on the basis of real-time concurrent biosignals as indicators of a user´s affective state (i.e., physiological reactions during a MR experience, measured by means of heart rate, skin temperature, electrodermal activity or electroencephalography) (Sanchez-Vives & Slater, 2005). Presence may be a driver of motor learning and could therefore play a vital role in virtual rehabilitation.

1.4.2 Virtual rehabilitation

Virtual environments are popular treatment approaches in rehabilitation settings and the evidence for VR-based interventions continues to grow (Aminov et al., 2018; De Rooij et al., 2016; Doumas et al., 2021; Laver et al., 2017; Lohse et al., 2014; Staiano & Flynn, 2014). VR-based rehabilitation, or virtual rehabilitation, refers to a broad spectrum of interventions ranging from highly immersive rehabilitation-specific to commercially available non-specific technologies, such as movement controlled active videogames (Levac & Galvin, 2013; Lohse et al., 2014). Virtual rehabilitation considers the VR system as a tool that is used by the clinician in therapy who needs to be competently trained and knows how to apply it in order to target patient goals, identify challenges, monitor and document the progress and outcomes (Levac & Galvin, 2013; Lohse et al., 2013). Virtual rehabilitation offers a multi-sensory and interactive experience that has the potential to target a wide range of motor and cognitive issues, with various advantages over traditional rehabilitation approaches (Rizzo & Kim, 2005; Schultheis & Rizzo, 2001).

Advantages of virtual rehabilitation

MR-based rehabilitation systems provide an experiential learning experience and can enhance observational learning, allow for a systematic manipulation of training, give the options to individualize and customize motor learning, augment feedback, enable home-based therapy, and allow for quantitative assessment, performance measurements, and the recording, analysis and monitoring of data. Moreover, it is a safe, ecologically valid, time- and cost-efficient option (Islam & Brunner, 2019; Rizzo & Kim, 2005; Schultheis & Rizzo, 2001; Teo et al., 2016). Further, virtual environments may influence a patients affective state and improve adherence with therapy (Teo et al., 2016), e.g., by increasing motivation to participate in training (Lohse et al., 2014), being more engaged in a certain task (Lohse et al., 2016) and having more fun during the intervention compared to traditional approaches (Laver et al., 2017; Saposnik et al., 2016). One of the core rationales for the integration of VR in neurorehabilitation after acquired brain damage is to promote motor and cognitive rehabilitation by facilitating neuroplasticity (Laver et al., 2017; Teo et al., 2016). Ideally, the VR intervention should augment conventional therapy by applying the principles of neurorehabilitation that enhance motor learning and recovery, e.g., providing high-intense and task-specific training in an enjoyable environment (Doumas et al., 2021; Levin et al., 2015). In contrast to off-the shelf recreational VR or AVG systems (e.g., commercial games provided by Nintendo Wii or Microsoft Kinect), those specifically designed for rehabilitation have been shown to have a higher impact on recovery, body function, and activity post-stroke (Aminov et al., 2018; Darekar et al., 2015; De Rooij et al., 2016; Laver et al., 2017; Maier, Rubio Ballester, et al., 2019), presumably as a result of incorporating neurorehabilitation principles (Doumas et al., 2021; Maier, Rubio Ballester, et al., 2019) or well-designed gaming mechanics (such as rewards, difficulty/challenge, feedback, choice/interactivity, clear goals/mechanics, and socialization) (Lohse et al., 2013). However, the focus of VR interventions, involving a variety of interacting components, has been predominantly on studies demonstrating an effect or differentiating the intervention from traditional approaches and less on *why* they work (Lohse et al., 2014). Thus, the active ingredients in virtual environments, that uniquely support its use within post-stroke rehabilitation are still unclear (Maier, Rubio Ballester, et al., 2019; Perez-Marcos, 2018).

Active ingredients in virtual rehabilitation

Levac and colleagues (Levac et al., 2012) investigated potential active ingredients in interactive computer play interventions used to promote motor outcomes in children with neuromotor impairments, and categorized them according the properties of the system or game (i.e., opportunities for practice, task specificity, flexibility to individualize, feedback, social play equalization, characteristics of the game, and comparisons to real-world), the effectiveness of the intervention on the user (i.e., neuroplastic changes, problem-solving, motivation), or the role of the therapist in the intervention (i.e., role of a support person). The authors concluded that the majority of the identified active ingredients still require research to evaluate their hypothesized effects on outcomes (Levac et al., 2012). Recently, Maier et al. (2019) identified six neurorehabilitation principles implemented in rehabilitation specific VR systems that seem to play a major role in influencing upper limb motor recovery post-stroke via enhanced neural plasticity: task-specific practice (e.g., ADL relevant training), variable practice (e.g., random and variable training), increasing difficulty (i.e., individualization), explicit feedback (e.g., knowledge about results), implicit feedback (e.g., knowledge about performance), and promotion of affected limb training (e.g., counteracting compensation and learned non-use) (Maier, Rubio Ballester, et al., 2019).

Another more frequently discussed rational for virtual rehabilitation is that the heightened affective experience in virtual environments facilitates recovery (Darekar et al., 2015). However, little is known yet in how affective factors contribute to VR-based motor learning post-stroke, and is therefore addressed within this thesis (see chapter 2, p.21). Further, the use of AR in rehabilitation has been studied, which is by far a less widespread technology than VR but with an arguably bigger potential for the integration of meaningful and task-specific training scenarios.

Augmented reality in rehabilitation

AR has already been implemented in various fields, where holographic elements enrich the perception of the real environment, including education, simulation and marketing, maintenance and training in industrial or military contexts, entertainment and gaming, telecommunication and medical applications (Kim et al., 2018). Within the medical field, next to applications targeting educative training, intra-operative navigation or guided surgery, there is a growing and ongoing interest in applications focusing on rehabilitation (Chen et al., 2017). Existing AR systems within physical rehabilitation range from simple to more complex technologies with an apparent focus on virtual cueing (e.g., virtual lines projected on the floor to cue walking) in neurological conditions, such as Parkinson´s Disease, Multiple Sclerosis, Cerebral Palsy or stroke (Al-Issa et al., 2012). AR is suggested to be a safe and promising tool for delivering a motor training in a more contextually relevant environment for patients' post-stroke (Gorman & Gustafsson, 2020), however, at this stage no conclusive recommendations can be given due to the early stages of available applications and a lack of evidence (Gorman &

Gustafsson, 2020). In fact, the use of AR systems within rehabilitation is still at the beginning as compared to VR applications (Al-Issa et al., 2012; Gorman & Gustafsson, 2020). Recently, since the development of stand-alone HMD-based AR systems (e.g., Figure 2), the interest in using AR-based cues for real time visual feedback during training (e.g., balance rehabilitation for the stroke population (Lee et al., 2019)) or for guided practice within the home environment (e.g., in the form of assistive devices for cognitive rehabilitation (Wolf et al., 2019)), has further been grown. The latter field of interest has also been subject of research within this dissertation, investigating the opportunities of AR-based guidance systems and of HMD-based holographic cueing as potential digital solutions for home-based rehabilitation and support.

1.4.3 Digital therapeutics

As described, MR-based approaches that make use of VR, videogames and AR have been developed to stimulate cortical reorganization and augment plasticity in neurologically impaired patients as well as to enable continued training in the home environment and telerehabilitation. With increasing levels of evidence and more affordable hardware devices they are expected to play a major role in the future of digital therapeutics (DTx) (Statista, 2022). DTx, i.e., evidence-based interventions using *high-quality software* (DTA, 2019), is a subsection of digital health, that describes a health system using digital technologies, platforms, and systems to augment healthcare effectiveness, including robotics and artificial intelligence, mobile phone applications, VR and telemedicine (Choi et al., 2019; Recchia et al., 2020). Accelerated by the COVID-19 pandemic, digital health represents an emerging and innovative area of therapy in 2021 by reducing costs, overcoming social inequalities, and improving diagnostic and treatment processes (Mantovani et al., 2020). DTx considers a software solution as medicine, e.g., a *digital drug* targeting a particular condition (Recchia et al., 2020). The difference to pharmacological drugs is the nature of the active ingredient being an algorithm, not a chemical or protein molecule (Recchia et al., 2020). In Germany, since the realization of the Digital Care Act ("Digitales Versorgungsgesetz") in 2019, medical doctors are officially allowed to prescribe DTx to publicly-insured patients and receive reimbursement equivalent to a traditional treatment. Currently, 31 Digital Health Applications (Digitale Gesundheitsanwendungen/DiGAs) have been approved by the BfArM $ 139e SGB V (BfArM, 2022), including "Rehappy" which consists of an app, a movement tracker and a web portal aiming to optimally guide, activate and inform patients post-stroke (Rehappy, 2021) and “Invirto” which enables people with agoraphobia, panic disorder or social phobia to receive treatment for their anxiety disorder from home by means of virtual reality (Invirto, 2022). The development of DTx and its medicalization is still in its infancy facing a number of challenges, including privacy concerns and regulatory frameworks for safety, efficacy and reimbursement (Choi et al., 2019). Still, the number of people using DTx worldwide is expected to raise from 22,5 million in 2020 to around 625 million in 2025 (Statista, 2022).

Chapter 2

Methods

2. Methods

Table 1 gives an overview of the four publications defining this dissertation, structured according to the Population-Intervention-Comparison-Outcome-Type of Study (PICOT) framework (Schardt et al., 2007). The first study focused on VR technology as part of a scoping review, studies II-IV were of experimental nature addressing AR technology by making use of the HoloLens device (Microsoft, 2021). Ethical approval for the experiments was obtained from the Ethics Committee of the Medical Faculty of the Technical University of Munich (TUM, reference number 175/17 S). All patients/participants or their legal representatives provided their written informed consent prior to testing, which was performed in accordance with the declaration of Helsinki. Besides being addressed in each article, this chapter provides a brief overview of the overall research questions, central methods and materials used within each study, with an emphasis on: 1) the software development processes, 2) the tasks being investigated, and 3) the performance analyses of the experiments.

Table 1. Overview of the performed studies defining this dissertation.

Study	Population	Intervention	Comparison	Outcome(s)	Type
I	Post-stroke adults	VR/AVG for motor skill improvement	Any	Impact of user affect on motor learning	Scoping Review
II	AD (n=10)	AR-cueing in ADL task (tea making)	Natural ADL task (tea making) - Same sample (n=10)	Feasibility/ Usability; Performance & qualitative content analysis	Mixed method design: Randomized crossover trial & interviews
III	Healthy young adults (n=32)	AR-cueing in SWI-paradigm	Standard SWI paradigm - Healthy age-matched CG	Heaviness Rating, Fingertip forces	Randomized controlled trial
IV	Post-stroke adults, LBD (n=25)	AR-cueing in PTU	Standard PTU task - Healthy age-matched CG (n=24)	Performance analysis, Sense of presence	Randomized crossover design

Abbreviations: AD= Alzheimer´s Disease, ADL = Activities of Daily Living, AR = Augmented Reality, AVG = Active Video Games, CG = Control Group, LBD = Left Brain Damage, PTU = Pantomime of Tool Use, SWI = Size Weight Illusion, VR = Virtual Reality

Mixed reality hardware used for experimental studies

The experiments performed within this dissertation (studies II-IV) were designed to investigate the opportunities of holographic[1] cueing in order to gather knowledge about how external holographic cues are treated by the sensorimotor system and to define the most beneficial type of AR cue for patients with cognitive impairment and apraxia. For that purpose, the Microsoft HoloLens (Microsoft, 2021) was chosen as a state-of-the-art technology that would enable freedom of movement for users while still possessing the ability to deliver support through its built in MR technology, e.g., users perform a certain task while receiving embedded support in the form of holographic objects and cues designed to guide users towards a successful outcome. HoloLens was the first fully self-contained, untethered head-mounted display running Windows 10, including an inertial measurement unit (IMU; accelerometer, gyroscope, and magnetometer), and four environment understanding sensors: 1) one depth camara with an 120°x120° angle of view, 2) one photographic video camera, 3) a four-microphone array, and 4) an ambient light sensor. Interactions are possible with the interface using three different control strategies: hand gestures, a handheld clicker or voice command (Bechtle; Microsoft, 2021).

Figure 2. Microsoft HoloLens (generation 1) used as a medium to investigate holographic cueing in studies II-IV. (Copyright: Nina Rohrbach / TUM).

[1] Holograms consist of light points that are projected into the user's field of view. Within this dissertation a hologram is defined as to the perception of a computer-generated object through stereo imaging.

2.1 Scoping Review methodology

The goal of the first study was to explore the impact of affective constructs (motivation, engagement, enjoyment, immersion, presence) on motor learning post-stroke because a greater understanding would enhance the clinical rationale for VR/AVG use and inform directions for subsequent research in that field (Rohrbach, Chicklis, et al., 2019). Table 2 offers definitions of the five constructs of interest to this scoping review.

For that purpose, the scoping review methodology was chosen as an ideal form of knowledge synthesis about that exploratory research question aiming to map the current field of literature (Colquhoun et al., 2014). Scoping reviews follow a methodological framework consisting of six stages that are useful to systematically examine the extent, range, and nature of the evidence of a topic, and address questions beyond effectiveness in order to describe how a particular field has been conceptualized or studied (Colquhoun et al., 2014; Tricco et al., 2018). As such, scoping reviews include a variety of sources but do not necessarily assess the quality of the reviewed studies but rather aim to generate an output linked to the review question. The scoping review within this dissertation was conducted according the original methodological framework proposed by Arksey and O`Malley (Arksey & O'Malley, 2005) and the updated recommendations proposed by Levac et al. (Levac et al., 2010) (Table 3), including a numerical summary and a summative content analysis as part of stage 5 (see additional file 2 and 3 published in (Rohrbach, Chicklis, et al., 2019)). Further, the review follows the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) reporting guidelines, that is a minimum set of items to include in research reports to increase methodological transparency and uptake of findings (Tricco et al., 2018).

Table 2. Affective construct definitions.

Construct	Definition
Motivation	Motivation encourages action toward a goal by eliciting and/or sustaining goal-directed behavior (Lohse et al., 2016).
Engagement	A cognitive and affective quality or experience of a user during an activity (Lohse et al., 2016).
Enjoyment	The state or process of taking pleasure in something (Merriam-Webster).
Immersion	The extent to which the VR system succeeds in delivering an environment which refocuses a user's sensations from the real to a virtual world (Rose et al., 2018; Weiss et al., 2006).
Presence	The psychological product of technological immersion (Bohil et al., 2011).

Note: this table was published in Rohrbach et al. (2019).

Table 3. Scoping review framework stages according Colquhoun et al. (2014).

Framework stages	Description
#1 Identifying the research questions	1. Despite the broad nature of the review (in order to examine and summarize breadth), clearly define the research question that will guide the scope including concept, target population, and health outcomes of interest 2. Determine the research question in conjunction with the purpose for conducting the scoping review. Use the rationale for the scoping review to help to determine the purpose 3. Stipulate the outputs (e.g., framework, list of recommendations) that will be the result of the review
#2 Searching for relevant studies	1. Identify relevant studies and develop a search strategy (where, which terms, sources, time span, and language) guided by the research question and purpose. Sources include electronic databases, reference lists, hand searching of key journals, and organizations and conferences 2. Comprehensiveness and breadth are important, thus, justify all decisions for limiting the scope and acknowledge any potential limitations to the study 3. Ensure the research team has the content and methodological expertise
#3 Selecting studies	1. Study selection is not linear, but rather an iterative process involving searching the literature, refining the search strategy, and reviewing articles for inclusion 2. Decision-making for study selection can be supported by the following steps: • Initial team meeting to discuss eligibility criteria • Two researchers should independently review abstracts and full text articles • When disagreements occur, incorporate a third reviewer to determine final inclusion • Hold reviewer meetings at the beginning, midpoint and final stages to discuss challenges and uncertainties, refine the search strategy if needed

#4 Charting the data	1. Collectively develop a data charting form and determine which variables to extract to answer the research question 2. Charting the data is an iterative process in which data are continually extracted and updated on the data charting form 3. Pilot the charting form on five to ten studies with two authors to determine whether the approach to data extraction is consistent with the research question and purpose 4. A qualitative content analysis may be required to extract contextual or process-oriented data
#5 Collating, summarizing, and reporting the results	Undertake three steps: 1. Analyze data, including descriptive numerical summary analysis and qualitative thematic analysis 2. Report the results, including the outputs as defined in stage #1 3. Discuss the findings as they relate to the study purpose and implications for future research, practice and policy
#6 Consultation (optional)	1. The value of consultation should be considered 2. The process of this optional stage should include: • A clear purpose for the consultation • Use preliminary findings to inform the consultation • Clearly articulate the type of stakeholders to consult, how data will be collected, analyzed, reported and integrated within the study • Incorporate opportunities for knowledge transfer and exchange with stakeholders in the field

2.2 Therapy Lens Project – holographic support in daily activities

Most existing assistive technologies that automate components of therapy are focusing on screens and projection-based systems (see 1.3.4 Assistive technologies). Instead, an HMD-based AR application could function as a unique way to compensate cognitive impairment by offering non-obtrusive holographic guidance in everyday life (Wolf et al., 2019), with the huge advantage of customizing the virtual stimuli to the individual patient´s needs and preferences (Palacios-Navarro et al., 2016). The Therapy Lens project (TherapyLens, 2021), an EIT Health (https://eithealth.eu) funded EU project led by TUM (Chair of Human Movement Science) in collaboration with IMEC (https://www.imec-int.com/en), RWTH Aachen University (https://cybernetics-lab.de), MaDoPA (http://www.madopa.fr) and CapDigital (https://www.capdigital.com), was driven by the vision of using HMD-based AR technology to extend and improve support and rehabilitation of patients with neurological diseases at home by specifically focusing on ADL for independent living. Within that framework, a prototype AR application was developed which is available online (TherapyLens). The prototype consists of seven key features that are designed to support patients with ADL at home: 1) three orientation games aiming to introduce the HMD (HoloLens) and software application to the users (e.g., how to interact with holograms), 2) a tea making tutorial game (Figure 3A), 3) a competitive memory game to challenge and improve short term memory skills (Figure 3B), 3) a tagging feature providing holographic reminders that are embedded in the user´s real environment (Figure 3C), and 4) a real tea making support feature (Figure 3C).

Figure 3. Therapy Lens application (Rohrbach & Armstrong, 2017). Three features are shown: A) holographic action guidance in a tea making tutorial, B) gamified holographic memory training supported by an avatar, C) holographic cues superimposed on real objects.

2.2.1 Software development

The Therapy Lens software was designed for HoloLens using the game engine development tool, Unity 3D version 2015.6 and was developed within a human-centered design, that is "an approach to interactive systems development that aims to make systems usable and useful by focusing on the users, their needs and requirements (…)" (ISO, 2019). Overall, feedback from six main iterative cycles with field tests in Germany, France and Belgium, involving the key stakeholders (23 patients with chronic neurological diseases, 12 elderly, 4 carers and 21 clinicians) resulted in the final prototype. Each test cycle incorporated an introduction (aim of the study, presentation of the device, explanation of control strategies, informed consent), the prototype testing, and semi-structured interviews. The co-design process allowed to identify barriers early within the development process and to adapt the prototype based on the feedback from the key stakeholders (Rohrbach & Armstrong, 2017; Rohrbach et al., 2017). The first cycles with dementia patients and carers were conducted in their home environment to gain a better understanding of their actual needs and preferences (Figure 4) (Meiland et al., 2017). The clinical experts were tested within either the clinic or the lab.

Figure 4. Co-design development process. A subject wearing the HoloLens device in the home environment is shown as part of the Therapy Lens app development process in Munich, Germany. The participant provided consent for the use of the images. (Copyright: Nina Rohrbach / TUM)

2.2.2 AR supported tea making task

The usability and feasibility of the integrated AR-based ADL support feature (i.e., tea making task) was tested within a cross-over trial design as part of this doctoral thesis and resulted in a publication presented in chapter 3 (Rohrbach, Gulde, et al., 2019). Patients with AD prepared a cup of tea twice, once in a natural way and once being supported by multidimensional cues delivered through the HoloLens headset (Figure 5; including holographic, auditive, and textual cues) for the following seven steps:

1. Fill water into the kettle
2. Switch the kettle on
3. Add a tea bag to the mug
4. Wait for the water to boil
5. Pour the hot water into the mug
6. Remove the tea bag
7. Task is finished

Figure 5. Experimental setup in study II. A patient is preparing a cup of tea supported by multidimensional cues delivered through the HoloLens glasses; i.e., animated holographic objects, text and audio information that direct the next step (Rohrbach, Gulde, et al., 2019). The participant provided consent for the use of the image. (Copyright left picture: Nina Rohrbach / TUM).

2.2.3 Performance analysis

The performance of patients was video-recorded and evaluated based on mixed methods to contextualize the quantitative findings using qualitative data (Östlund et al., 2011).

Quantitative analysis

The quantitative analysis included clinical data (i.e., age, Mini Mental State Examination (Folstein et al., 1975) - MMSE score) and performance related data (i.e., order of condition, trial durations, the success rates and number or errors performed (see Table 4 for details on the underlying error analysis).

Qualitative analysis

The qualitative data were evaluated applying a structured content analysis of semi-structured interviews with patients (Kuckartz, 2016). After a word-for-word transcription of the audio recordings using the software f4/f5 (dr. dressing & pehl GmbH), the software MAXQDA Analytics Pro 2018 (Release 18.0.0, VERBI GmbH) was used to code the interview data and extract thematic summaries (Appendix).

Table 4. Error taxonomy for the tea making task based on Bieńkiewicz et al. (2015).

Error	**Definition**	**Category**
Addition	Adding an extra component action	Sequencing errors
Anticipation	Action performed earlier than usual	
Perseveration	Unintentional repetition	
Perplexity	Delay or hesitation	
Sequence	Action performed later than usual	
Sequence Omission	Subtask not performed	
Ingredient Omission	Failing to add an ingredient	Conceptual errors
Ingredient Substitution	Unintended ingredient is used	
Misestimation	Using too much/little of substance	
Object Substitution	Unintended object is used	
Quality	Action is carried out inappropriately	
Execution	Error in the execution of the task	Spatio-temporal errors
Mislocation	Action is performed in the wrong place	

2.3 Augmented Size Weight Illusion – holographic cueing in real object interactions

Illusion can be defined as “an instance of a wrong or misinterpreted perception of a sensory experience” (LEXICO, 2021). The famous Size Weight Illusion (SWI) describes the robust phenomenon that small objects feel heavier than large objects, even though being adjusted to have the same mass. In addition, they are initially lifted at a lower rate of force (Charpentier, 1891). MR systems allow users a natural view on their physical environment including real-time estimation of the position of the hand when performing manual tasks (Rho et al., 2020), and provide a unique platform for manipulating perceptions (Perez-Marcos, 2018), however, there is not much knowledge yet about how humans perceive and interact with virtual cues. The idea behind this experiment was to investigate whether the SWI could be influenced by manipulating the visual-perceptual context, specifically, by creating another visual illusion using AR technology. The goal was to examine whether physical boxes of different sizes and overlaid with holographic boxes (which appeared to be identically-sized, Figure 6B) would eliminate this robust perceptual effect and overwhelm the normal propensity to grip and lift these boxes with distinct forces (Rohrbach, Hermsdörfer, et al., 2021). We hypothesized the virtual cues to override the real cues and expected that participants would experience the identically sized objects as having the same mass and that they would lift objects with similar rates of force. When performing the lifting task (Figure 6), participants are required to perceptually integrate the holographic cube with the grip force manipulandum. Having this in mind, the sense of presence (Table 5) was administered to gather information about the experienced realness, spatial presence and perceptual stress evoked by the holograms.

2.3.1 Software development

Unity 3D version 2017.4 (Unity Technologies 2019) was used to design the application for HoloLens. Vuforia (Vuforia Engine 2018) was integrated into the Unity Framework which provides a stable tracking functionality along with direct plugins for the HoloLens camera. Vuforia allows to recognize QR-codes (here embedded with slightly transparent holographic cubes) in the user´s field of view that were attached to the physical cubes (Figure 6), and thus scale and align the holographic cubes relative to the real cubes even when being moved. Videos of the holographic stimuli can be accessed via the Open Science Framework (OSF) https://osf.io/fz368/.

2.3.2 AR supported lifting task

Participants repeatedly lifted two cubes of equal (390g) weight but different size (big cube 10.0 cm × 10.0 cm ×10.0 cm; small cube 6.3 cm × 6.3 cm × 6.3 cm) and reported the perceived heaviness. The cubes were attached to a manipulandum capable of measuring grip forces, load forces and 3-dimensional accelerations (Figure 6C). Figure 6 depicts the experimental setup in the AR supported lifting group, where participants received virtual cues in the form of three-dimensional holographic cubes giving the illusion that both cubes were having the equal size.

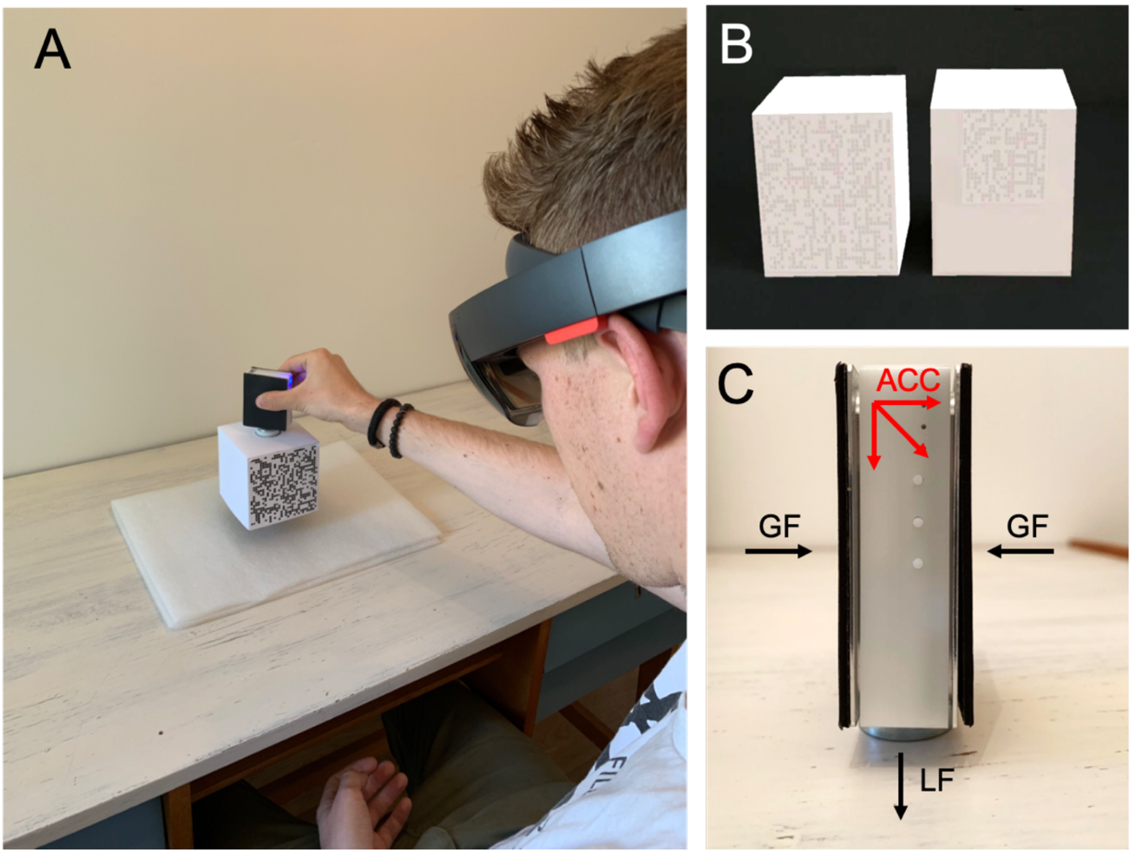


Figure 6. Experimental setup in study III. A) A participant is lifting a cube attached to the grip force manipulandum (C) while receiving a holographic size cue (B) that is delivered via a QR code and recognized by the HoloLens glasses. Note: ACC = Acceleration, GF = Grip Force, LF = Load Force. The participant provided consent for the use of the image. Copyright: Nina Rohrbach / TUM

2.3.3 Performance analysis

The performance was analysed by a customized software (GFWin, MedCom, Munich) collecting grip force data, numerical ratings of heaviness, and the sense of presence induced by the holograms.

Fingertip force rates

Prior to initial lift-off, fingertip force rates (peak grip force rates, GFR; and peak load force rates, LFR) were measured to determine how the holographic cues influenced sensorimotor prediction.

Heaviness ratings

After each lift, verbal reports about the experienced heaviness indicated how the holographic cues influenced the SWI.

Presence Questionnaire

A presence questionnaire consisting of seven questions that were answered on a 7-point Likert scale, examined the elements of realness, spatial presence and perceptual stress (Table 5) (Regenbrecht & Schubert, 2002).

Table 5. Presence questionnaire based on Regenbrecht & Schubert (2002).

Component	Question
Realness	Q1: Was watching the virtual objects (cubes) just as natural as watching the real world?
	Q2: Did you have the impression that the virtual objects (cubes) belonged to the real object (grip force manipulandum), or did they seem separate from it?
	Q3: Did you have the impression that you could have touched and grasped the virtual objects (cubes)?
Spatial presence	Q4: Did the virtual objects (cubes) appear to be (visualized) on a screen, or did you have the impression that they were located in space?
	Q5: Did you have the impression of seeing the virtual objects (cubes) as merely flat images or as three-dimensional objects?
Perceptual stress	Q6: Did you pay attention at all to the difference between real and virtual objects (cubes)?
	Q7: Did you have to make an effort to recognize the virtual objects (cubes) as being three-dimensional?

2.4 Augmented Pantomiming – holographic cue evaluation

The goal of the last experimental study was to investigate whether the disturbed movement execution in patients after left brain damage (LBD) with apraxia could be mitigated by AR stimulation. The hypothesis was, if visual stimuli facilitate the access to the appropriate motor program, the performance should improve with cues of higher saliency and more contextual information. For that purpose, patients were supported with virtual cues with different degrees of saliency during a well-established pantomiming task, and in such, identify the most beneficial way of augmenting contextual visual information.

2.4.1 Software development

Five virtual objects (hammer, key, iron, watering can, bulb) were created as part of the pantomime task and presented either in a screen environment or an HMD environment (HoloLens), either in a static or dynamic fashion (Figure 7). The testing environments were designed using the game engine development tool Unity 3D version 2017.4 (Unity Technologies 2019). In order to generate very realistic looking objects, the real objects were 3D scanned and animated with motion capture recordings from real tool use movements (Qualisys Inc., Gothenburg, Sweden). The holographic objects were further adjusted in space to maintain the object´s real size and positioned in space that the tools´ handle functioned as an easy to graspable stimulus. Videos showing the screen-based and HMD-based versions of the objects in static and dynamic conditions can be accessed via the Open Science Framework (OSF; https://osf.io/uakw2/). The full project code is available at GitHub https://github.com/Ninarohrbach/panto-holo.

Figure 7. Virtual tool development. On the basis of real objects and motion capture analysis (A) five virtual objects were created and (B) animated. Copyright: Nina Rohrbach / TUM

2.4.2 AR supported pantomime of tool use task

The pantomime of tool use task requires the subject to produce an action without holding the object in the hand and is a very sensitive test in detecting the presence of limb apraxia (Goldenberg et al., 2003). LBD patients and healthy control participants mimed the use of the five objects, three times in a row, supported by the different visual cues. In the AR supported condition, participants wore the HoloLens headset showing the holographic versions of the tool, either in a static or animated way (Figure 8). After performing all testing conditions (screen static, screen dynamic, HMD static, HMD dynamic), patients were asked to show use of the five objects while holding the real physical tool.

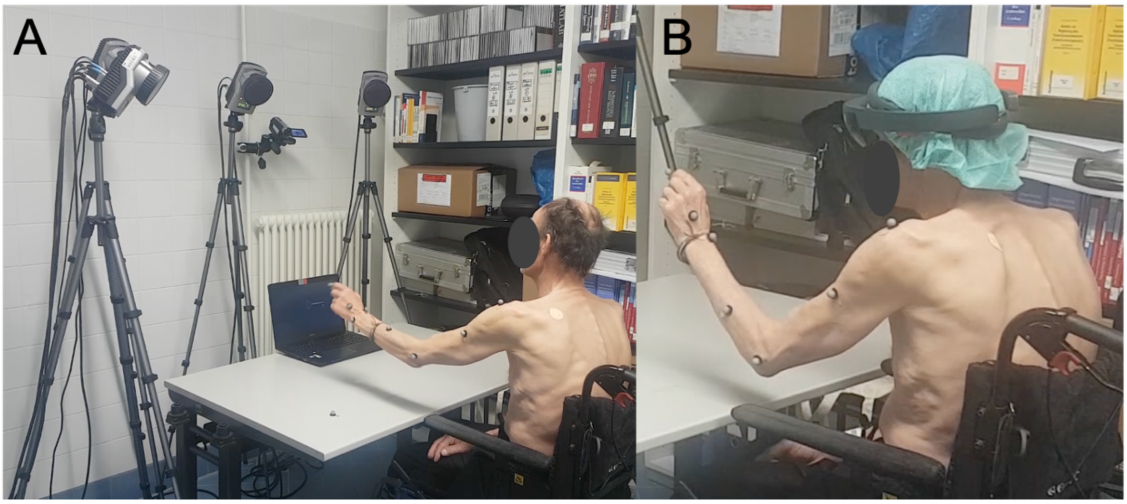


Figure 8. Experimental setup in study IV. A participant is showing how to mime the use of a key. Spherical markers attached to the upper limb are detected by the four motion capture cameras. A) The patient receives visual cues via a screen. B) The patient receives holographic cues via a head mounted display (HoloLens). The participant provided consent for the use of the images. Copyright: Nina Rohrbach / TUM

2.4.3 Performance analysis

Video recordings and motion capturing (a spherical marker attached to the subject´s left back of the hand) using four cameras (Oquus, Qualisys Inc., Gothenborg, Sweden) served to analyze the participants performance (Figure 8).

Video analysis

The most predominant methodology for analyzing apraxic behavior are video recordings of the performance and the classification of action errors as presented in Table 4. For the purpose of this experiment a scoring system was applied rating the performance of each participant (Randerath et al., 2017). The *Production scale* served to analyze for the presence or absence of predefined movement components using a 3-point scale (0 = incorrect, 1=distorted, 2=correct), resulting in a maximum score of 24 points per object and condition after three times. The *Interaction scale* was applied to capture the interaction with the virtual objects (0 = no interaction, 1 = interaction), i.e., when participants tried to reach forward, grasp or follow the movements of the animated versions, resulting in a maximum score of 3 points per object and condition after three trials.

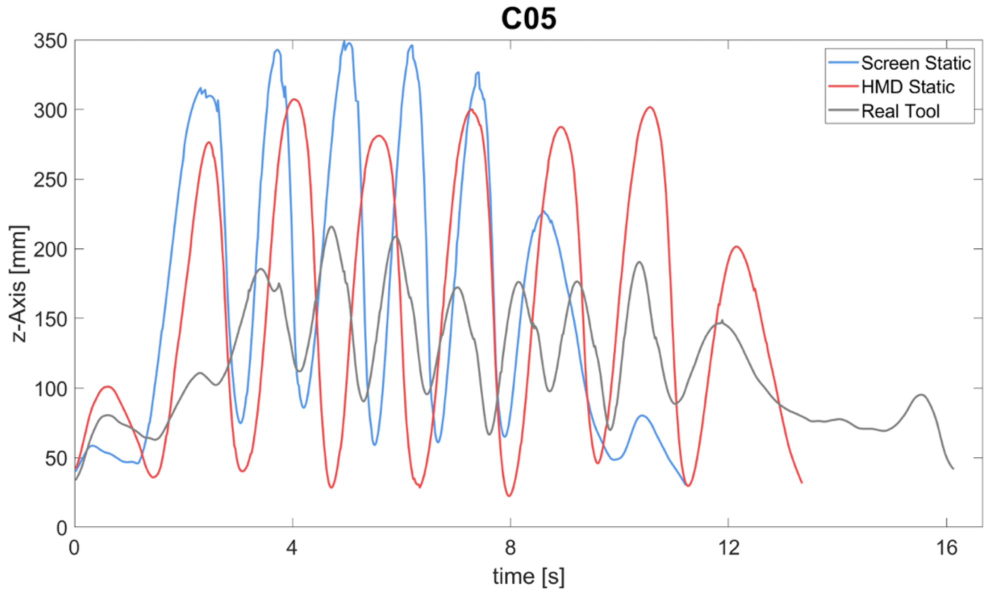
Table 6. Applied scoring system for the pantomime of tool use task.

PRODUCTION SCALE		
Movement component	**Description**	**Error examples for distorted movements**
Grip formation	Manipulation knowledge of the object is essential.	Grip incomplete, too narrow, too wide
Movement content	Requires successful retrieval of the matching movement and its integration into a movement plan.	Movement produced by wrong body part
Movement orientation	Recognition of movement goal and purpose is needed.	Missing distance to the table
Spatial orientation	Correct orientation of the movement and the hand in space.	Hand in the wrong plane
INTERACTION SCALE		
Description	Participant actively tries to reach forward, grasp or follow the virtual object	

Note: The table has been published as supplementary data in Rohrbach et al. (2021).

Kinematic analysis

The kinematic approach served as a visualization for the error analysis of the hammer performance (repetitive up and down movement). Post-processing was performed using MATLAB R2018b (MathWorks, Natick, MA, USA). The starting and the ending time points were determined by calculating the overall marker velocity in 3D space and thresholding it at v_{th}=0.012 [m/s]. The vertical axis of the movement was extracted and plotted for visualization (e.g., Figure 9).



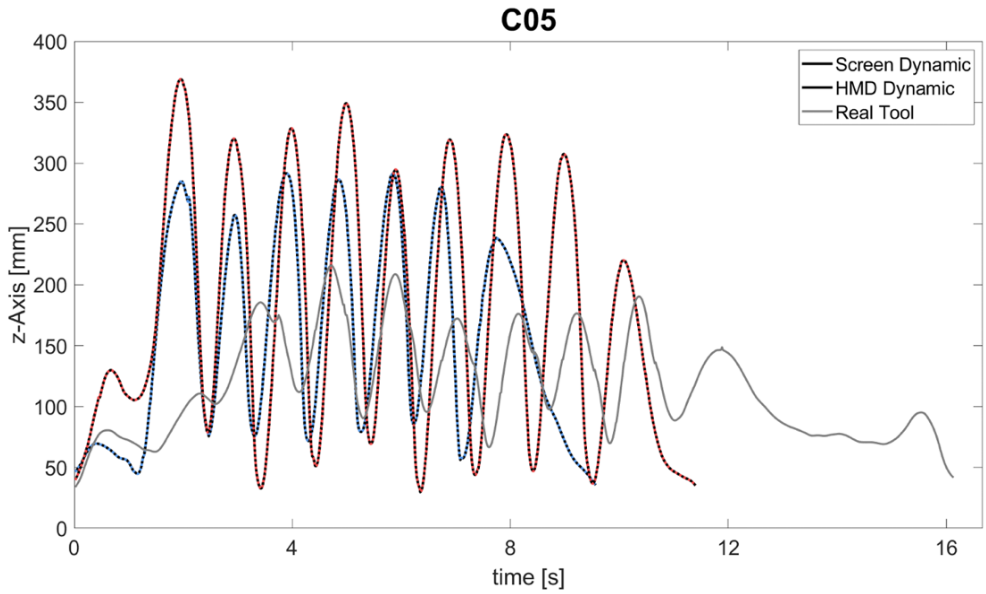


Figure 9. Kinematic analysis of hand movements. Exemplarily display of a movement trajectory in 3D space of a healthy control subject (C05) performing the hammering movement supported by static virtual cues (upper graph) and dynamic virtual cues (lower graph). Red ink represents the screen environment. Blue ink represents the HMD environment. The complete trajectory along the z-Axis (in mm) is shown.

Clinical data

Table 7 shows the series of clinical tests that were collected and analysed as part of this experiment.

Table 7. Overview of the performed clinical tests in study IV.

Test	**Area of assessment**
Mini Mental State Examination (MMSE) (Folstein et al., 1975)	Cognitive impairment
Titmus Test (House Fly test, Circles test)	Stereovision
Edinburgh Handedness Inventory (EDI) (Oldfield, 1971)	Dominance of a person's hand in everyday activities before the stroke
Nine Hole Peg Test (NHPT) (Mathiowetz et al., 1985)	Manual dexterity
Motricity Index (MI) (Demeurisse et al., 1980)	Upper extremity function, functional mobility
Diagnostic Instrument for Limb Apraxia – Short Version (DILA-S) (Randerath et al., 2017)	Presence and severity of apraxia
Presence Questionnaire (PQ) (Regenbrecht & Schubert, 2002) *	Sense of presence

**Note: Question 2 (see Table 5) has been removed within this study.*

Chapter 3

Publications

3. Publications

This section presents the four publications defining this dissertation, including a visual abstract, a reprint of the abstracts of each study, a statement on the authors' contributions and the original publications. All studies have been published under the Open Access Creative Commons Attribution License (CC-BY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Table 8 summarizes the four articles published as part of this dissertation.

Table 8. List of publications defining this dissertation.

Study	Title	Authors	Journal	Date of Publication
I	What is the impact of user affect on motor learning in virtual environments after stroke? A scoping review	Rohrbach, N. Chicklis, E. Levac, D.E.	Journal of Neuroengineering and Rehabilitation	27 June 2019
II	An augmented reality approach for ADL support in Alzheimer's disease: a crossover trial.	Rohrbach, N. Gulde, P. Armstrong, AR. Hartig, L. Abdelrazeq, A. Schröder, S. Neuse, J. Grimmer, T. Diehl-Schmid, J. Hermsdörfer, J.	Journal of Neuroengineering and Rehabilitation	3 June 2019
III	Fooling the size–weight illusion—Using augmented reality to eliminate the effect of size on perceptions of heaviness and sensorimotor prediction.	Rohrbach, N. Hermsdörfer, J. Huber, L-M. Thiefelder, A. Buckingham, G.	Virtual Reality	20 March 2021
IV	Improvement of apraxia with Augmented Reality: influencing pantomime of tool use via holographic cues	Rohrbach, N. Krewer, C. Löhnert, L. Thiefelder, A. Randerath, J. Jahn, K. Hermsdörfer, J.	Frontiers in Neurology – Neurorehabilitation	26 August 2021

3.1 What is the impact of user affect on motor learning in virtual environments after stroke? A scoping review

3.1.1 Visual abstract

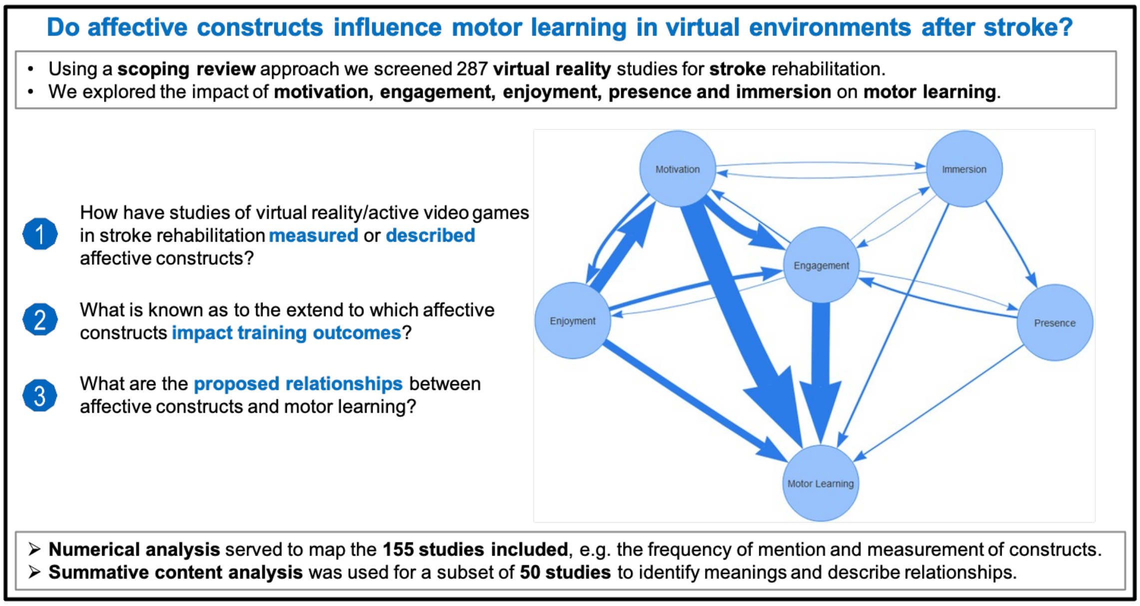


Figure 10. Visual abstract study I.

Authors: Nina Rohrbach, Emily Chicklis, Danielle Elaine Levac

Title: What is the impact of user affect on motor learning in virtual environments after stroke? A scoping review

Journal: Journal of Neuroengineering and Rehabilitation

DOI: https://doi.org/10.1186/s12984-019-0546-4

Protocol: The protocol was registered with the Open Science Framework (OSF, https://osf.io/3x6y5/) on 8 November 2017 after the development of the search strategy and before data extraction and analysis.

Citation: Rohrbach, N., Chicklis, E., & Levac, D. E. (2019). What is the impact of user affect on motor learning in virtual environments after stroke? A scoping review. *Journal of neuroengineering and rehabilitation*, *16*(1), 1-14.

3.1.2 Summary

Purpose: The purported affective impact of virtual reality (VR) and active video gaming (AVG) systems is a key marketing strategy underlying their use in stroke rehabilitation, yet little is known as to how affective constructs are measured or linked to intervention outcomes. The purpose of this scoping review is to 1) explore how motivation, enjoyment, engagement, immersion and presence are measured or described in VR/AVG interventions for patients with stroke; 2) identify directional relationships between these constructs; and 3) evaluate their impact on motor learning outcomes.

Methods: A literature search was undertaken of VR/AVG interventional studies for adults post-stroke published in Medline, PEDro and CINAHL databases between 2007 and 2017. Following screening, reviewers used an iterative charting framework to extract data about construct measurement and description. A numerical and thematic analytical approach adhered to established scoping review guidelines.

Results: One hundred fifty-five studies were included in the review. Although the majority (89%; N = 138) of studies described at least one of the five constructs within their text, construct measurement took place in only 32% (N = 50) of studies. The most frequently described construct was motivation (79%, N = 123) while the most frequently measured construct was enjoyment (27%, N = 42). A summative content analysis of the 50 studies in which a construct was measured revealed that constructs were described either as a rationale for the use of VR/AVGs in rehabilitation (76%, N = 38) or as an explanation for intervention results (56%, N = 29). 38 (76%) of the studies proposed relational links between two or more constructs and/or between any construct and motor learning. No study used statistical analyses to examine these links.

Conclusions: Results indicate a clear discrepancy between the theoretical importance of affective constructs within VR/ AVG interventions and actual construct measurement. Standardized terminology and outcome measures are required to better understand how enjoyment, engagement, motivation, immersion and presence contribute individually or in interaction to VR/AVG intervention effectiveness.

3.1.3 Authors´ contributions

The results of this study are based on an international collaboration between the Northeastern University, Boston (Department of Physical Therapy, Movement & Rehabilitation Sciences, Rehabilitation Games and Virtual Reality laboratory) and TUM (Chair of Human Movement Sciences). Nina Rohrbach is the first author and Danielle Levac the corresponding author of this manuscript. All authors contributed to the final draft of the manuscript, read and approved the final manuscript.

Nina Rohrbach: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – Original draft, Writing – Review & Editing, Visualization

Emily Chicklis: Validation, Formal analysis, Visualization

Danielle Levac: Conceptualization, Methodology, Validation, Investigation, Formal analysis, Writing – Original draft, Writing – Review & Editing, Supervision, Project administration

3.1.4 Original publication I

Rohrbach *et al. Journal of NeuroEngineering and Rehabilitation* (2019) 16:79
https://doi.org/10.1186/s12984-019-0546-4

Journal of NeuroEngineering and Rehabilitation

REVIEW Open Access

What is the impact of user affect on motor learning in virtual environments after stroke? A scoping review

Nina Rohrbach[1], Emily Chicklis[2] and Danielle Elaine Levac[2*]

Abstract

Purpose: The purported affective impact of virtual reality (VR) and active video gaming (AVG) systems is a key marketing strategy underlying their use in stroke rehabilitation, yet little is known as to how affective constructs are measured or linked to intervention outcomes. The purpose of this scoping review is to 1) explore how motivation, enjoyment, engagement, immersion and presence are measured or described in VR/AVG interventions for patients with stroke; 2) identify directional relationships between these constructs; and 3) evaluate their impact on motor learning outcomes.

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Conclusions: Results indicate a clear discrepancy between the theoretical importance of affective constructs within VR/AVG interventions and actual construct measurement. Standardized terminology and outcome measures are required to better understand how enjoyment, engagement, motivation, immersion and presence contribute individually or in interaction to VR/AVG intervention effectiveness.

Keywords: Virtual reality, Stroke, Motor learning, Motivation, Enjoyment, Engagement, Immersion, Presence, Scoping review

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Introduction

An increasing evidence base supports the use of virtual reality (VR) and active video gaming (AVG) systems to promote motor learning in stroke rehabilitation [1–4]. However, practical and logistical barriers to VR/AVG implementation in clinical sites have been well described [5–7]. To support their use, researchers and developers often emphasize the potential advantages of VR/AVG systems over conventional interventions, including that these technologies may enhance a patient's affective experience in therapy for the purpose of facilitating recovery [8–11]. Examining the role of affective factors for motor learning is an emerging area of emphasis in rehabilitation [2, 12–15].

VR/AVG use may enhance patients' motivation to participate in rehabilitation as well as their engagement in therapeutic tasks. Motivation encourages action toward a goal by eliciting and/or sustaining goal-directed behavior [16]. Motivation can be intrinsic (derived from personal curiosity, importance or relevance of the goal) or extrinsic (elicited via external reward) [17]. Engagement is a cognitive and affective quality or experience of a user during an activity [16]. Many characteristics of VR/AVG play can contribute to user motivation and engagement, such as novelty, salient audiovisual graphics, interactivity, feedback, socialization, optimal challenge [14], extrinsic rewards, intrinsic curiosity or desire to improve in the game, goal-oriented tasks, and meaningful play [18].

Motivation and engagement are hypothesized to support motor learning either indirectly, through increased practice dosage leading to increased repetitive practice, or directly, via enhanced dopaminergic mechanisms influencing motor learning processes [15, 16]. Yet evidence is required to support these claims. A logical first step is to understand how these constructs are being measured within VR/AVG intervention studies. Several studies have used practice dosage or intensity as an indicator of motivation or engagement [19–21]. To the authors' knowledge, few have specifically evaluated the indirect mechanistic pathway by correlating measurement of patient motivation or engagement in VR/AVGs with practice dosage or intensity. While participants in VR/AVG studies report higher motivation as compared to conventional interventions [22–24], conclusions regarding the relationship between motivation and intervention outcomes are limited by lack of consistency and rigour in measurement, including the use of instruments with poor psychometric properties [22, 23].

The body of research exploring the *direct* effects of engagement or motivation on motor learning is still in its infancy. Lohse et al. [16] were the first to evaluate whether a more audiovisually enriched as compared to more sterile version of a novel AVG task contributed to skill acquisition and retention in typically developing young adults, finding that participants who played under the enriching condition had greater generalized learning and complex skill retention. Self-reported engagement (User Engagement Scale; UES) was higher in the enriched group, but the only difference in self-reported motivation was in the Effort subscale of the Intrinsic Motivation Inventory (IMI), where the enriched group reported less effort as compared to the sterile group. The authors did not find a significant correlation between engagement, motivation and retention scores. A follow-up study using electroencephalography did not replicate the finding that the more enriched practice condition enhanced learning, it did show that more engaged learners had increased information processing, as measured by reduced attentional reserve [25].

Enjoyment, defined as 'the state or process of taking pleasure in something' [26], has less frequently been the subject of study in motor learning research, but has become popular as a way of describing patient interaction with VR/AVGs. Enjoyment may be hypothesized to be a precursor to both motivation and engagement. Given that the prevailing marketing of VR/AVGs is that they are 'fun' and 'enjoyable' [1, 3, 14, 27], it is important to evaluate its measurement in the context of other constructs.

Motivation, engagement and enjoyment in VR/AVGs may be influenced by the additional constructs of immersion and presence. Immersion is defined as "the extent to which the VR system succeeds in delivering an environment which refocuses a user's sensations from the real world to a virtual world" [13, 28]. Immersion is considered as an objective construct referring to how the computational properties of the technology can deliver an illusion of reality through hardware, software, viewing displays and tracking capabilities [29, 30]. A recent systematic review [13] could not conclusively state effect of immersion on user performance. Immersion is distinct from presence, defined as the "psychological product of technological immersion" [31]. Presence is influenced by many factors, including the characteristics of the user, the VR/AVG task, and the VR/AVG system [28]. While presence is thought to be related to enhanced motivation and performance [32], relationships between this and other constructs of interest require exploration. Table 1 outlines definitions of constructs of interest to this scoping review.

The purpose of this scoping review is to explore the impact of these affective constructs on motor learning after stroke. This greater understanding will enhance the clinical rationale for VR/AVG use and inform directions for subsequent research. Specifically, our objectives were to:

1. Describe how VR/AVG studies measure or report client enjoyment, motivation, engagement, immersion and presence.
2. Evaluate the extent to which motivation, enjoyment, engagement, immersion, and presence impact motor learning.

Table 1 Construct definitions

Construct	Definition	Reference
Motivation	Motivation encourages action toward a goal by eliciting and/or sustaining goal-directed behavior.	[16]
Engagement	Engagement is a cognitive and affective quality or experience of a user during an activity.	[16]
Enjoyment	The state or process of taking pleasure in something.	[26]
Immersion	The extent to which the VR system succeeds in delivering an environment which refocuses a user's sensations from the real world to a virtual world.	[13, 28]
Presence	The psychological product of technological immersion.	[31]

3. Propose directional relationships between enjoyment, motivation, engagement, immersion, presence and motor learning.

Methods

Scoping reviews synthesize knowledge about an exploratory research question to map a field of literature [33]. They are useful methodologies to address questions beyond effectiveness and to describe how a particular subject has been conceptualized or studied [33]. The study is structured according the original methodological framework for conducting scoping reviews [34] and the updated recommendations proposed by Levac et al. [35]. The updated methodological framework consists of six stages: stage 1) Identifying the research question; Stage 2) Searching for relevant studies; 3) Selecting studies; 4) Charting the data; 5) Collating, summarizing, and reporting the results, and 6) Consulting with stakeholders to inform or validate study findings. The consultation stage is optional and was omitted here. The review follows the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) reporting guidelines [36].

Protocol and registration

The protocol was registered with the Open Science Framework on 8 November 2017 (OSF, http://osf.io/3x6y5) after the development of the search strategy and before data extraction and analysis.

Stage 1. Identifying the research questions

Our research questions (RQ) were as follows:

RQ1: How have studies of VR/AVGs in stroke rehabilitation measured or described motivation, enjoyment, engagement, immersion or presence?
RQ2: What is known as to the extent to which motivation, enjoyment, engagement, immersion and presence impact training outcomes?
RQ3: What are the proposed relationships between motivation, enjoyment, engagement, immersion, presence and motor learning?

Stage 2. Identifying relevant studies

Information sources CINAHL Complete, MEDLINE, and PEDro were searched for articles published from 2007 up to November 2017. This timeline was chosen on the basis of the rapid development in the field following the release of the active video gaming system Nintendo Wii/WiiFit in 2007. The specific search strategy was created by one author (NR) and peer reviewed by another author (DL) with expertise in conducting scoping reviews. A combination of medical sub-headings (MeSH) and key words on "stroke" and "virtual reality", were adapted as needed for each database and combined using boolean operators.

Search The MEDLINE search strategy is exemplarily presented in Additional file 1: Table S1 (Date of last search: Friday, October 13, 2017 4:16:49 PM).

Stage 3. Study selection

Eligibility criteria The Population-Intervention-Comparison-Outcome (PICO) approach was applied to systematically define our eligibility criteria. Inclusion criteria were studies of any design published in the last 10 years in English or German describing rehabilitation interventions using virtual reality (VR) and/or active video games (AVG) including both commercially available systems (i.e. Nintendo Wii console, Sony PlayStation or Xbox Kinect consoles) and custom designed games for stroke rehabilitation (including interfaces such as hand-held controllers, gloves, treadmill, etc.) for motor skill improvement in adult patients with stroke. We did not specifically search for studies measuring any of the five constructs. We included studies with any type of control as long as data provided for stroke population were reported separately. Exclusion criteria were robot-based interventions and robot-assisted training (exoskeletons, fixed manipulandum), functional electrical stimulation/transcranial current stimulation; brain computer interface, electromyography-controlled interventions; outcomes other than motor-based (i.e. energy expenditure, metabolism, cognitive, memory, communication, neglect), and usability/reliability studies, reviews or meta-analyses. Robotic devices, even those that include VR simulations, were excluded due to the additional potential influences on our constructs of interest resulting from the physically assistive nature of these devices.

Selection of sources of evidence

Prior to the formal screening process, a calibration exercise with two reviewers (JZ, NR) on a subset of articles ($n = 10$) was undertaken to pilot the screening questions and eligibility criteria. Based on that calibration exercise, the first selection was made by title and abstract screening of each study by one reviewer (NR). Studies that did not meet the eligibility criteria on the basis of the content of their abstracts were excluded. If required, the full-text versions were obtained to determine whether the studies met our eligibility criteria. In case of uncertainty, another reviewer (DL) blind to the first reviewers' comments reviewed the study. Any disagreements concerning the inclusion/exclusion were collaboratively discussed until the authors met consensus. Figure 1 outlines the study selection process [37].

Stage 4. Charting the data

Data charting process Data from the identified studies were extracted using a charting framework developed a priori by the authors. The charting framework was pilot-tested with a random sample of five articles to check agreement among reviewers. As a result of this process, charting rules were developed to guide a group of five reviewers, including the original two (NR, DL, KP, JZ, MS), who independently charted data from each eligible article. The construct 'enjoyment' was added following data extraction from the first 50 papers, as reviewers noted that it was a frequently mentioned construct and should be included in the review; these papers were re-reviewed. The full process required frequent review and discussion within the core research team (NR, EC, and DL) to resolve any uncertainties, and ensure that data extraction was in line with the research questions. All charted data from each reviewer was reviewed by one of the authors (NR). EndNote X8 was used as a reference management software and to avoid multiple reports of the same study. Microsoft Excel was used to manage data within the review team.

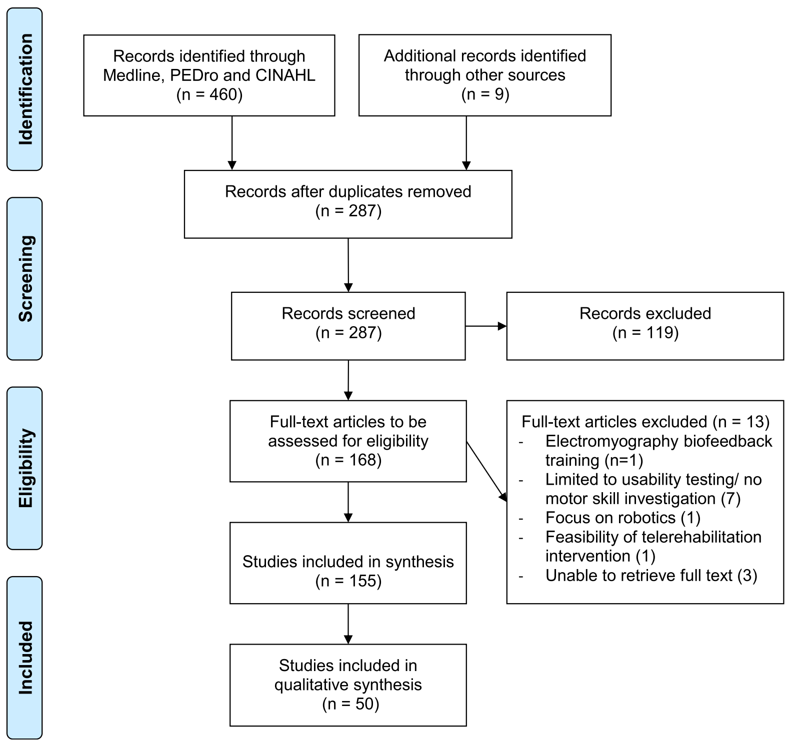

Fig. 1 Flow chart depicting the selection process of identified articles

Data items The main data extracted were 1) study characteristics (journal name, year of publication, study design, type of VR/AVG technology, study sample, duration of intervention); 2) text in which the author mentioned or described each of the five constructs (motivation, enjoyment [also described as 'fun'], engagement, immersion, presence); 3) nature of measurement of any of the five constructs (inferential or qualitative), and 4) text related to the authors' proposed relationships between the constructs.

Characteristics and critical appraisal of individual sources of evidence We did not appraise the methodological quality or risk of bias of the included studies, which is consistent with guidance on scoping review conduct [36].

Stage 5. Collating and summarizing the results

Synthesis of results Numerical analysis (counts, frequencies, proportions) was used to map the studies included in the review in terms of study design, type of VR/AVG system and viewing medium, intervention focus (upper vs lower extremities vs postural control), frequency of mention of constructs, and frequency of measurement of constructs. In a first step, we screened the articles for the constructs of interest (if, and where, the construct was mentioned). In a second step, the studies that mentioned one or more constructs were checked to clarify whether and how the authors measured these constructs (Additional file 2). If measurement was undertaken, the article was included for further analysis (Additional file 3). A numerical summary was used to describe the frequency and type of inferential statistics per construct, and the results of the statistical analyses were summarized. Summative content analysis [38] of the authors' construct description within the text was undertaken for the subset of studies in which a construct was measured. The goal of summative content analysis is to understand and identify how words are used in context (in this case, we were interested in the specific labels of each of our 5 constructs) [38]. In addition to counting frequencies of use, this approach interprets how words are used and how they relate to each other. Summative content analysis was also used to identify how authors' described relationships between motivation, engagement, enjoyment, immersion, presence and motor learning in their texts. This analysis resulted in frequency counts of each relationship, which we illustrated in a Fig. 2.

Results

Selection of sources of evidence

Figure 1 outlines the study selection process.

Overview of the included studies

The articles included in this review employed a range of methodologies: 45.2% were Randomized Controlled Trials (RCTs, $n = 70$), 18.7% were pilot-studies ($n = 29$), 9.7% were pilot-RCTs ($n = 15$), 10.3% used a pre-post design ($n = 16$), 5.8% were case reports/series ($n = 9$), and 10.4% ($n = 16$) applied other designs such as mixed-methods, interviews, non-randomized controlled or crossover trials, overviews of

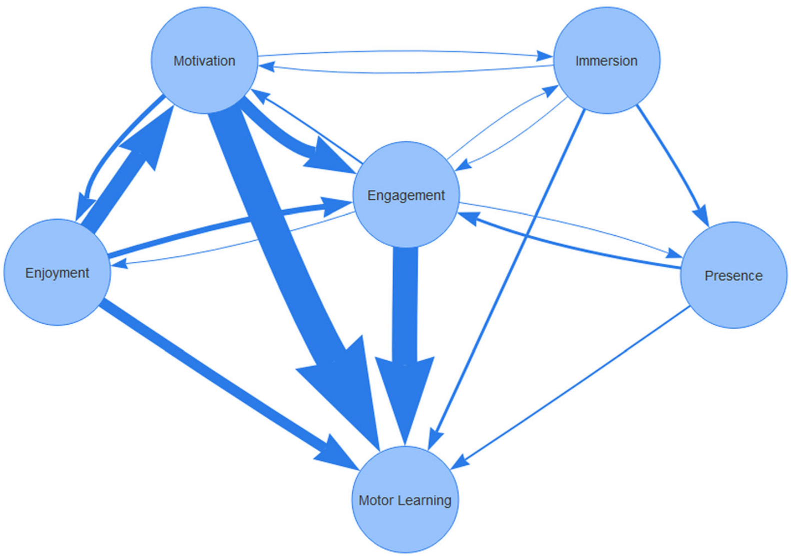

Fig. 2 Proposed relationships between the five constructs and motor learning

work, case control or descriptive observational studies. Table 2 illustrates that most studies (47%, $n = 73$) involved customized, rehabilitation-specific devices in which tracking/interaction took place indirectly via a controller (e.g., the YouGrabber system) or directly via motion capture (e.g., using the Microsoft Kinect sensor) and visual display of the virtual environment was on a 2D flat-screen monitor, while only 5 % of studies ($n = 8$) investigated any type of stereoscopic glasses or head mounted display. Most (66.45%) of included studies ($n = 103$) focused on upper extremity impairments after stroke while 29.67% ($n = 46$) focused on lower extremities/balance and 3.8% focused on both ($n = 6$). Additional File 2 provides a complete list of the 155 studies included in the review.

RQ1: How have studies of VR/AVGs in stroke rehabilitation described or measured motivation, engagement, enjoyment, presence or immersion?

One hundred fifty-five studies were included in the review. 89% ($n = 138/155$) of studies mentioned at least one of the five constructs within their text, but only 32% ($N = 50/155$) measured a construct using a standardized or non-standardized outcome measure (Table 3).

Table 4 lists the outcome measures used per construct. Examples of standardized measurements include the Intrinsic Motivation Inventory (IMI) and the Presence Questionnaire (PQ). Self-designed questionnaires were applied in 15 studies, where authors mostly used Likert scales or dichotomous yes/no answer formats to evaluate motivation, engagement and enjoyment/fun. For example, Chen et al. [52] designed specific questions to assess motivation and enjoyment that were scored on a 5-point Likert-type scale, with 1 signifying “strongly disagree” and 5 being “strongly agree”. Another example can be found in Schuck et al. [53] who asked questions requiring yes/no answers such as “Was the game fun to play? Did the game increase your motivation to perform your exercise?”, Summative content analysis [38] of the authors’ construct description within the text was undertaken for the 50 studies in which a construct was measured. Additional File 3 provides a complete list of the 50 studies included in summative content analysis.

Table 2 VR classification

	Markerless/Motion Capture		Controller/Peripheral	
	Non-customized	Customized	Non-customized	Customized
Head mounted display	0	3	0	5
Screen/ projection	13	35	37	73
Stereoscopic 3D glasses	0	0	0	3

Table 3 Frequency of construct measurement and mention

	Mentioned/described	Measured
Motivation	123/155 (79.35%)	28/155 (18.06%)
Enjoyment/Fun	73/155 (47.09%)	42/155 (27.09%)
Engagement	65/155 (41.93%)	8/155 (5.16%)
Immersion	47/155 (30.32%)	4/155 (2.58%)
Presence	17/155 (10.96%)	6/155 (3.87%)

Two themes emerged from the content analysis. In the first theme, represented in 76% of studies ($n = 38/50$), authors described the construct as a rationale for use of VR/AVGs in rehabilitation. In the second theme, represented in 58% of studies ($n = 29/50$), authors used the construct to explain why the VR/AVG intervention was successful. The two themes are described below. Table 5 depicts the quantitative breakdown of both themes for each individual construct.

Theme 1: Construct described as a rationale for use of VR/AVG Each of the five constructs was described under this theme. Engagement and motivation were described almost identically. Authors described engagement as a rationale for VR/AVG use because of its potential to influence practice dosage and adherence, greater amounts of which were felt to promote functional improvements [19, 20, 56, 57, 68]. Motivation was also described as a rationale for use of VR/AVG interventions for its potential to increase training intensity, influencing motor learning and neuroplasticity [20, 39, 41–45, 49, 60]. The ability to motivate clients in this way was identified as unique to this treatment method [40, 42, 45, 48]. Rationales presented for VR/AVG use included the potential to engage and motivate users by involving them in game selection [20] or individualization of game features [46], the ability to elicit multiplayer competition or cooperation [39, 44, 48] the provision of individualized challenge [21, 44, 48, 54, 57], and the delivery of feedback [43, 45, 50, 53, 61, 62, 73] or of a rewarding sense of achievement [45, 55]. For example, Subramanian et al. [49] stated that “*Motivation and interactivity of the VE were enhanced by the added visual effects and game score that enabled participants to track success.*”

The potential for VR/AVG use to increase patient enjoyment was described as a strong rationale for use in rehabilitation. Specifically, authors outlined patient enjoyment related to playing games [60, 62, 64, 66, 70–72, 82] which differed from traditional rehabilitation approaches (e.g. [52, 73]. Enjoyment was also seen as essential to the flow experience induced by VR/AVG play [57, 72]. Flow was defined as the *“feeling of complete and energized engagement in an activity, with a high level of enjoyment and fulfillment”* and described as supportive

Table 4 Name and frequency of outcome measures used per construct

Construct	Outcome Measurements	Frequency (N)	References
Motivation	IMI	12	[20, 39–49]
	BDI	2	[50, 51]
	Self-designed Questionnaires[a]	6	[48, 52–56]
	Flow-Questionnaire	1	[57]
	Time system was used	1	[21]
	Interviews/Comments/Surveys	10	[21, 42, 50, 58–64]
Enjoyment/Fun	Sub-scale of IMI (Interest/enjoyment)	10	[20, 39–45, 47, 48]
	Self-designed Questionnaires[a]	12	[49, 52–54, 65–72]
	Flow-Questionnaire	1	[57]
	PACES	1	[73]
	SFQ	3	[74–76]
	Interviews/Comments/Surveys	16	[50, 58–62, 64, 66, 68, 77–82]
Engagement	Self-designed Questionnaires[a]	2	[56, 68]
	Interviews/Comments/Surveys	5	[20, 60, 61, 68, 83]
	Diaries (training time and duration)	1	[20]
	PQ (involvement items: 5,6,10,23,32)	1	[19]
	Training time	1	[19]
	Flow-Questionnaire	1	[57]
Immersion	ITQ	1	[78]
	SFQ	2	[76, 84]
	PQ (involvement items: 5,6,10,23,32)	1	[19]
Presence	ITQ	1	[78]
	SFQ	4	[74–76, 84]
	PQ (involvement items: 5,6,10,23,32)	1	[19]

IMI Intrinsic Motivation Questionnaire, *BDI* Beck Depression Inventory with four sections: cognitive, emotive, motivational, physiological; [a] e.g. VAS/Likert format, *PACES* Physical ACtivity Enjoyment Scale, *PQ* Presence Questionnaire, *ITQ* Immersive Tendencies Questionnaire, *SFQ* Short Feedback Questionnaire

of adherence to VR/AVG-based rehabilitation [72]. Enjoyment was described as facilitating motivation [20, 39–45, 47–49, 68, 74], engagement [57, 68, 78], and training intensity [42, 60, 66, 79] in VR/AVG use. Finally, patient enjoyment due to rewards and feedback provided in VR/AVG games was described as a rationale for their use in clinical practice [57, 66, 78].

Immersion was described as a rationale for VR/AVG use because of its influence on user performance and the fact that it differentiates VR/AVG interventions from conventional rehabilitation [76, 84]. Similarly, authors described presence as an essential component separating the advantages of VR/AVG use over other interventions [75, 76, 78, 84]. All authors interpreted immersion as a subjective characteristic, i.e. defining it as *"the perception of the setting as real"* [76, 84], or *"the feeling of being in the virtual world, rather than looking at it"* [78]. For example, Crosbie et al. [78] stated: *"A person with a positive immersive tendency* [as measured by the ITQ instrument] *may be more likely to be successful in the performance of virtual tasks."* Authors also described the need to

Table 5 Quantitative summary of summative content analysis

	Measured	Theme 1: Construct mentioned as a rationale for use of VR/AVG	Theme 2: Construct mentioned as an explanation for successful intervention
Motivation	28/155	21/28 (75%)	23/28 (82.1%)
Enjoyment/Fun	42/155	25/42 (59.52)	17/42 (40.47)
Engagement	8/155	5/8 (62.5%)	5/8 (62.5%)
Immersion	4/155	4/4 (100%)	0/4 (0%)
Presence	6/155	4/6 (66.7%)	0/6 (0%)

measure side effects associated with immersion to justify the burden of VR/AVG use [19, 78, 84].

Theme 2: Construct described as an explanation for successful intervention Motivation, enjoyment and engagement were the only constructs described under this theme. Engagement and motivation were described as contributing to intervention success by promoting adherence and contributing to a higher training intensity [20, 41, 43, 47, 48, 52, 55, 58] as well as by distracting participants'from therapeutic intent [50, 60]. For example, Lewis et al. [68] state that *"the level of engagement and motivation in performing tasks is posited as factor in determining the success of rehabilitation interventions using VR"*. Another example is Sampson et al. [41] who describe that *"(…) perhaps the main benefit found in this study was that the VR system successfully motivated participants to practice using their affected arms and engage in and enjoy therapy for sustained periods of time."* Game design features such as individualized challenge levels [21, 42, 47, 48, 51–53, 57, 58, 61, 62], meaningful tasks [20, 52, 53, 57, 58], multiplayer platforms [39, 48], and feedback [42, 43, 46, 48, 49, 51, 52, 58, 61–63] were described as promoting motivation and influencing successful outcomes. For example, Friedmann et al. [43] suggested that *"...sensory-rich visual and auditory feedback motivated high effort levels"*.

Enjoyment achieved through VR/AVG play was described as important to intervention outcomes because it is a critical factor for rehabilitation success [53, 68, 72], lowers stress levels [49] and induces flow [57, 60, 72]. Enjoyment was also described as an explanation for the success of the interventions due to its effects on patient motivation and engagement [20, 45, 52, 64, 73], particularly in patients who otherwise lacked interest or motivation to complete normal exercise regimes [39, 58]. Gorsic et al. [48] stated enjoyment led to effort, stating that *"participants enjoyed competitive exercises more than exercising alone, and that this also increased self-reported effort put into the exercise."* Schuck et al. [53] referred their intervention success to previous literature *"that implicated the importance of fun, motivation, and engagement as critical factors for success in rehabilitation."*

RQ2: What do we know about the extent to which motivation, engagement, presence, enjoyment and level of immersion impact training outcomes?

While 74% of studies ($n = 37$) in which a construct was measured reported only descriptive statistics or qualitative summaries, 26% ($n = 13$) used inferential statistical analysis to evaluate hypotheses related to a construct in different arms of the intervention, e.g. to compare differences in motivation or enjoyment between two studied practice conditions [40, 42, 43, 45, 47, 49, 52, 65, 71, 73]. None of the studies used statistical inference to link any of the five constructs to motor learning outcomes.

RQ3: What are the proposed relationships between motivation, engagement, enjoyment, immersion, and presence and motor learning?

Summative content analysis was used to explore authors' interpretations of construct relationships in their texts. Figure 2 illustrates the frequency and direction of identified relationships.

The most frequently described relationship was motivation leading to motor learning ($N = 24$). For example, Hale et al. [80] state: *"One of the rationales for computer-based rehabilitation is the use of the motivational aspects of the technology to stimulate people to practice repetitive movement to facilitate neuroplasticity and enhance functional movement."* The second most frequently reported relationship was the influence of patient enjoyment on motivation ($N = 15$). Enjoyment is seen as *"a key factor for increasing motivation"* [74]. However, authors measured this construct using an instrument designed to assess motivation: the Intrinsic Motivation Inventory (IMI). For instance, Lloréns et al. [47] conclude: *"In terms of motivation, the results of the IMI showed that most of the participants found the system enjoyable (...)".*

The combination of two constructs was suggested to influence a third construct. For example, Kottink et al. [45] suggest that the combination of fun and motivation together lead to engagement, stating: *"The application of videogames in rehabilitation (rehab games) can be regarded as a specific form of VR training, in which the fun and motivational elements of the exercises are emphasized to engage people during their activity."* Multidimensional relationships, in which constructs are chained, are listed in Table 6.

For example, Flynn et al. [50] state that engagement and motivation lead to immersion and this impacts therapeutic outcomes: *"Moreover, the virtual environment (VE) provides an engaging and motivating framework for feedback allowing the participant to become immersed in the virtual world and to experience the emotional sense of "winning" in a particular game."* Turkbey et al. [64] suggest that enjoyment leads to motivation, which leads to engagement: *"It should be remembered that patients' enjoyment and belief in benefits of a treatment may improve engagement in a therapy and intensity of training as a reflection of increased motivation."* Finally, Hung et al. [73] also describe this relationship: *"One of the most important successes of the Wii Fit training may lie in the pleasure component, which motivates subjects to engage more fully in the program."*

Table 6 Construct relationships proposed by authors

Source	Destination 1	Destination 2	Destination 3	Frequency	References
Motivation	Motor Learning			24	[19, 20, 39, 42–45, 48–51, 53, 55, 57, 58, 60, 66–68, 71, 74, 76, 80, 84]
Motivation	Enjoyment			3	[41, 52, 61]
Motivation	Enjoyment	Motor Learning		2	[52, 61]
Motivation	Engagement			12	[19, 20, 41, 45, 46, 51, 57, 61, 64, 73, 79, 81]
Motivation	Engagement	Motor Learning		5	[20, 46, 57, 73, 79]
Motivation	Immersion	Motor Learning		1	[50]
Enjoyment	Motor Learning			6	[52, 53, 61, 68, 78, 80]
Enjoyment	Motivation			15	[20, 39–42, 44, 47, 49, 51, 62, 64, 66, 68, 73, 74]
Enjoyment	Motivation	Motor Learning		5	[42, 44, 66, 68, 74]
Enjoyment	Motivation	Engagement		4	[20, 51, 64, 73]
Enjoyment	Motivation	Engagement	Motor Learning	2	[20, 73]
Enjoyment	Engagement			6	[45, 49, 57, 68, 72, 78]
Enjoyment	Engagement	Motor Learning		3	[49, 68, 78]
Engagement	Motor Learning			13	[19, 20, 40, 46, 49, 50, 53, 57, 68, 73, 78, 79]
Engagement	Motivation			2	[57, 71]
Engagement	Motivation	Motor Learning		1	[71]
Engagement	Enjoyment			1	[60]
Engagement	Immersion	Motor Learning		1	[50]
Engagement	Presence			1	[40]
Immersion	Motor Learning			2	[50, 78]
Immersion	Motivation			1	[60]
Immersion	Engagement			1	[40]
Immersion	Presence	Engagement		2	[19, 50]
Immersion	Presence	Engagement	Motor Learning	1	[19]
Immersion	Presence	Motor Learning		1	[45]
Presence	Engagement	Motor Learning		1	[46]

Discussion

This scoping review explored how motivation, enjoyment, engagement, immersion and presence were described or measured in VR/AVG studies in stroke rehabilitation. We also sought to identify potential links between these constructs and motor learning outcomes. Although the majority of studies mentioned at least one of the five constructs within their text, construct measurement took place in only 1/3 of studies. Multiple relational links between two or more constructs or between any construct and motor learning were described, though statistical analyses were not used to examine these links.

The emphasis by authors on enjoyment was a surprising finding of this review. Enjoyment was described as important because it underlies both engagement and motivation, and because it is central to essential game design principles of VR/AVG games. However, although it was the most frequently measured construct, it is important to note that measurement of this construct was undertaken with the use of instruments designed for other purposes. This included using instruments measuring flow or intrinsic motivation [85, 86] or self-designed subjective questionnaires lacking psychometric properties [72]. Hung et al. [73] were the only ones to use an enjoyment-specific scale (PACES), although its psychometric properties have not yet been validated in the stroke population or for exercise modalities other than sports [87]. Given that authors appear to consider this construct foundational both to the affective impact of VR/AVGs and to the mechanics of game design, it will be important to achieve consensus on optimal measurement.

A second important finding of the review was the inconsistency with which constructs were mentioned, described, defined and measured in these studies, and the fact that despite lack of tests of statistical inference or even measurement, authors stated assumptions or conclusions about constructs as fact. For example, Shin et al. [57] conclude that their device "*encouraged the patient's skill development, improved immersion, and motivated further rehabilitation by providing meaningful* *play, optimal challenge, and a flow experience*" while acknowledging that they did not measure motivation. In addition, definitions did not consistently align with our a-priori understanding of the terms, and were often vague and interchangeable. Indeed, these terms are differentially operationalized and defined in various fields (e.g. psychology, sports medicine, rehabilitation). This issue of ill-defined terminology was identified by some authors [20]. For example, immersion was often described as a synonym for presence, as follows: "*This allows users to experience a high degree of immersion; they feel as if they are in the virtual world, rather than looking at it.*" [78] Presence was also described as an indicator of subjective immersion, for example in [19]: *"(...) presence is a subjective measure used in VR studies to quantify how immersed a user is in a VE."* Also problematic is the fact that authors use a single instrument to measure several different constructs. For example, immersion was measured using the Presence Questionnaire, the same instrument as that used to measure presence, which was also used to measure what authors' labelled as engagement [19]. Overall, the inconsistent and varying use of terms, as well as the use of single instruments to quantify different constructs presents a challenge for readers and should be addressed through the development of consistent terminology and a consensus on optimal outcome measures [20].

Among the studies in which a construct was measured, 44% of studies ($N = 22$) used validated instruments (e.g. IMI, IM-TEQ, PQ, ITQ, TSFQ, PACES and SFQ), however, most measures were not verified yet for the targeted purpose (e.g., the PACES), or population (e.g. PQ). Most used either indirect tools (e.g. taking training time or practice duration as a measure of motivation and engagement, $N = 3$), study-specific subjective questionnaires with untested psychometric properties ($N = 15$), or exclusively qualitative assessments (e.g. interviews or comments, $N = 12$) with varying rigour in data analysis (Table 4). Tatla et al. [22, 23] also found a lack of valid instruments used to measure motivation in pediatric interventions for children with cerebral palsy and acquired brain injury. As such, consensus is clearly required on instruments in order to align the field and facilitate interpretation and the advancement of knowledge. Existing instruments could be adapted and validated for use in VR/AVG interventions and with specific target populations. For example, Gil-Gómez et al. [88] have proposed the SEQ (Suitability Evaluation Questionnaire) that is based on the SFQ (Short Feedback Questionnaire) but has been updated to cover specific VR-related items.The use of direct or indirect objective measures of motivation, enjoyment, engagement is an option to overcome challenges of subjective self-report. Indirect measures include recording time spent interacting with the VR/AVG game (as undertaken by [19–21], counting the frequency of repetitions, or measuring the intensity of physical activity (for example, using EMG measurement, as in Zimmerli et al. who considered physical activity intensity as an indicator of engagement in VR/AVG interventions) [89]. Clearly, this indirect approach is not without limitations, as there will always be a multitude of influences besides affective state on adherence, dosage and intensity (for example, the expectation of external rewards, or the pressure to maintain a strict treatment schedule). As such, more direct objective measures are also warranted [20]. Examples include electroencephalography, including use of event related potentials to evaluate attentional demand [25], spectra analysis for indicators of engagement, or other measures such as galvanic skin response, heart rate variability or functional near-infrared spectroscopy [90]. The use of such objective measures may elucidate the neurophysiological processes by which affective state influences motor learning [25].

Perez-Marcos [91] suggests that authors should distinguish between VR hardware and software to evaluate user experiences. Specifically, authors should be more specific about describing the components of their VR/AVG interventions to differentiate between systems, the games themselves, and the resulting user experience [91]. Results of our review indicate that game mechanics such as rewards, feedback, challenge, choice/interactivity, clear goals, and socialization [14] were frequently lauded for their influence on motivation, engagement and enjoyment. These game design features are different from the features of the VR system that is delivering the intervention, and can likely be delivered across different platforms. Interestingly, authors did not link these game design features to immersion or presence, indicating that these constructs are more aligned with the game context than with the viewing medium or interaction modality. Further unpacking the 'active ingredients' of VR/AVG interventions, and how they may be attached to game characteristics as opposed to hardware components, is a key area for future research [92, 93].

Results of the review illustrate the discrepancy between the frequency of construct description or actual measurement. One potential explanation is that these constructs are universally accepted as inherent to VR/AVG interventions, and as such, researchers are not compelled to measure them. No conclusions can be made about the potential impact of motivation, enjoyment, engagement, degree of immersion and level of presence on the motor improvements achieved in a VE. We recommend including these analyses in future work, where power analyses permit. Such calculations should be facilitated as the field continues to grow and study designs move beyond the feasibility and pilot study stage in which authors' focus on demonstrating an effect or differentiating the intervention from traditional care.

Limitations

This scoping review had several limitations. We identified studies in which the apparent goal of VR/AVG interventions was motor skill improvement; however, the assumption of motor learning as an intervention goal was our own. We used summative content analysis to analyze article text, but did not record nor assign speculative or other intent to authors' words. As such, and particularly since no inferential statistics were performed in the original articles to support identified relationships, we can assign no weight to relational links identified in this review. While our literature search included the three main rehabilitation-specific databases, literature may have been missed from other databases. In particular, we did not search the IEEE Xplore database, which may have led to more studies on immersion and presence, though perhaps not in a rehabilitation context. In keeping with scoping review conduct recommendations, we did not undertake a quality appraisal of the included studies.

The construct of 'Flow' was mentioned in relation to motivation, enjoyment, engagement, and immersion, e.g. by stating that *"flow experience results from a combination of intrinsic motivation and complete immersion in the intervention"* [57] and flow was often described as an indicator of engagement [72, 94]. As such, the omission of flow as a construct relevant to affective state in VR/AVG interventions is a scoping review limitation. Finally, we did not differentiate our analyses between non-customized and customized rehabilitation-specific VR/AVG systems. Non-customized systems are less expensive and accessible, may be easier to use and are most frequently used in clinical practice [5]. Differentiating between these types of VR/AVGs may have helped to elicit any potential differences in the constructs that may be due to potentially more impactful game design principles (such as more abundant audiovisual feedback, or more explicit competition) of commercially-available games as compared to rehabilitation-specific games.

Next steps for research

Results of this scoping review indicate the need for greater consensus on definitions and terminology. Given the lack of psychometrically-valid outcome measures, integrating greater use of objective measures is essential. Researchers should include hypotheses as to how these constructs influence motor learning. High quality mixed methods research designs may be useful when appropriately conducted using a rigorous framework for design and interpretation [95], as a qualitative component can help to further elucidate what specifically participants found motivating or engaging, and can be used as a complement to explore the validity of self-report quantitative measures or objective measures. Finally, measuring sustainability and changes in these constructs over time can inform decision-making protocols for clinicians to better adjust VR/AVG intervention parameters to sustain motivation and engagement [23].

Greater understanding of the impact of affective state on learning will inform the design of VR interventions that can better exploit attributes found to promote motivation and engagement. Researchers can conduct experiments in VR to inform directions for development of VR-based therapeutic tasks, but they could also provide knowledge to inform conventional rehabilitation by providing greater awareness of the potential importance of affective state for learning. In addition, because VR experimental paradigms can better isolate or manipulate a single task presentation factor over others as compared to experiments in physical environments, this can support understanding of which specific factors enhance motivation and engagement for different types (e.g. ages, interests, cognitive abilities) of users. This can also provide more evidence for why therapists could consider using VR over traditional interventions as well as provide information for how to design conventional interventions that take advantage of these same attributes.

Conclusions

To accompany the increasing evidence of VR/AVG effectiveness in stroke rehabilitation, it is important to better understand factors that may differentiate certain systems or modulate effectiveness in clients with differing characteristics. The growing emphasis on the role of affective factors in motor learning combined with our findings that many researchers use these constructs as a rationale for VR/AVG use highlight the need to better understand and measure whether affective state differentiates VR/AVG use from traditional interventions and whether it contributes to intervention outcomes. This body of literature currently demonstrates a discrepancy between description and measurement, one that might be explained by the early stage of the literature and the current feasibility-oriented research methodologies. Results of the review provide suggestions for researchers interested in measuring these constructs and emphasize the need for consensus on terminology and outcome measures. Finally, the results point to the need to better understand, through improved measurement and inferential analyses, the potential impact of affective constructs and technical level of immersion on outcomes achieved through practice in VR environments.

Additional files

Additional file 1: Table S1. MEDLINE search strategy. (PDF 106 kb)

Additional file 2: List of studies included in synthesis (*n* = 155). (XLSX 31 kb)

Additional file 3: List of studies included in summative content analysis (*n* = 50). (XLSX 63 kb)

Abbreviations

AVG: Active Video Game; BDI: Beck Depression Inventory; IMI: Intrinsic Motivation Inventory; ITQ: Immersive Tendencies Questionnaire; OSF: Open Science Framework; PACES: Physical ACtivity Enjoyment Scale; PICO: Population-Intervention-Comparison-Outcome; PQ: Presence Questionnaire; PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses; RCT: Randomized Controlled Trial; RQ: Research Question; ScR: Scoping Review; SFQ: Short Feedback Questionnaire; UES: User Engagement Scale; VAS: Visual Analogue Scale; VR: Virtual Reality

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Authors' contributions

NR and DL formulated the research questions. NR and DL participated in the study selection process. NR, EC and DL performed the data extraction and data analysis. DL and NR drafted the manuscript. EC generated the Figures. All authors read and approved the final manuscript.

Authors' information

NR is a physical therapist (B.Sc.) and movement scientist (M.Sc.). She is a doctoral candidate in the Department of Sport and Health Sciences, Chair of Human Movement Science, at the Technical University of Munich. She holds a fellowship of the Centre of Digitisation.Bavaria which is a Germany-wide unique co-operation, research and entrepreneurship platform with the objective to increase the speed of digital innovations.

DL is a physical therapist and Assistant Professor in the Department of Physical Therapy, Movement and Rehabilitation Sciences at Bouvé College of Health Sciences, Northeastern University, with an affiliated position in the Department of Bioengineering. She directs the Rehabilitation Games and Virtual Reality (ReGameVR) Laboratory.

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Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Publisher's Note

3.2 An augmented reality approach for ADL support in Alzheimer´s disease: a crossover trial

3.2.1 Visual abstract

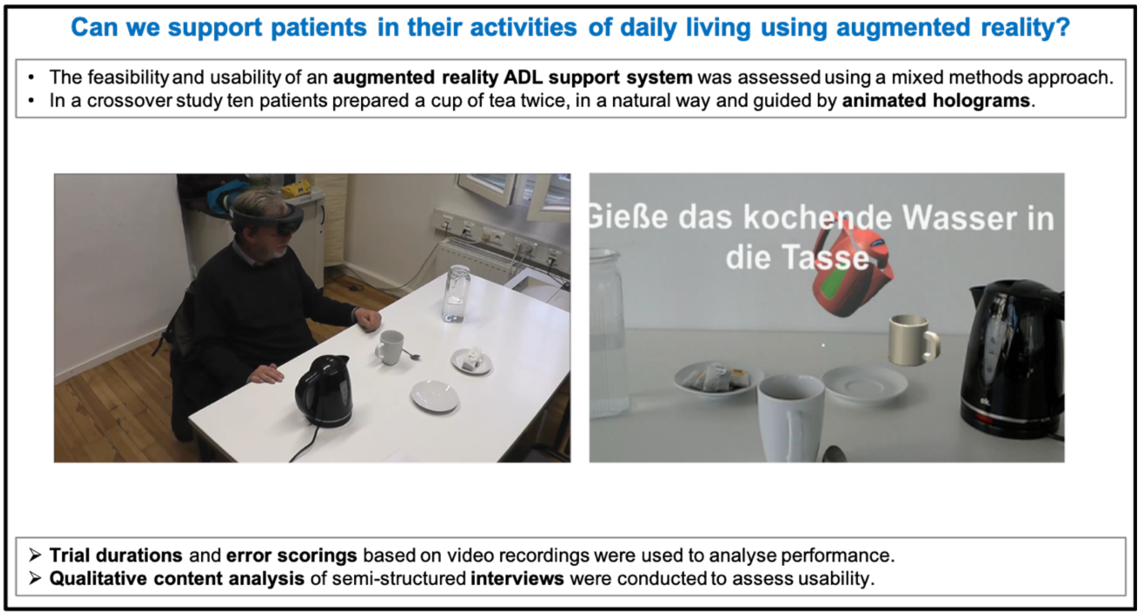

Figure 11. Visual abstract study II.

Authors: Nina Rohrbach, Philipp Gulde, Alan Robert Armstrong, Linda Hartig, Anas Abdelrazeq, Stefan Schröder, Johanne Neuse, Timo Grimmer, Janine Diehl-Schmid and Joachim Hermsdörfer

Title: An augmented reality approach for ADL support in Alzheimer’s disease: a crossover trial.

Journal: Journal of Neuroengineering and Rehabilitation

DOI: https://doi.org/10.1186/s12984-019-0546-4

Protocol: The protocol was retroprospectively registered with the German Clinical Trials Register (DRKS) on 11 June 2018 (Trial ID = DRKS00014870)

Citation: Rohrbach, N., Gulde, P., Armstrong, A. R., Hartig, L., Abdelrazeq, A., Schröder, S., ... & Hermsdörfer, J. (2019). An augmented reality approach for ADL support in Alzheimer’s disease: a crossover trial. Journal of neuroengineering and rehabilitation, 16(1), 1-11.

Website: www.therapylens.com

App: The final demo of the used prototype was published and is freely available on the Microsoft Store since February 2018 under the name Therapy Lens

3.2.2 Summary

Background: Dementia of the Alzheimer's type can impair the performance of activities of daily living and therefore severely impact independent living. Assistive technologies can support such patients when carrying out daily tasks.

Methods: In this crossover study, we used an augmented reality approach using a Microsoft HoloLens to support patients in a tea making task. During task execution, subjects received three-dimensional dynamic holograms of the sub-steps necessary to complete the task. Ten patients suffering from Alzheimer's disease were tested and post-hoc semi-structured interviews were conducted to assess usability.

Results: The patients committed errors when executing the task with and without holographic assistance. No differences in success rates or error frequencies were observed ($p_{success}$ = .250, p_{errors} = .887). Patients revealed prolonged trial durations (Glass' Δ = 1.475) when wearing the augmented reality headset. A model of multiple linear regression ($R^2_{adjusted}$ = .958) revealed an influence of the errors in the control condition and a moderation by the errors in the experimental condition. Patients with more severe problems in the natural performance of the task showed lower increases in trial durations when wearing the HoloLens.

Conclusions: We assume that the application was a secondary task requesting its own resources and impairing performance on its own. The regression suggests however that the given assistance was compensating these additional costs in patients with stronger needs of support. Interview data on usability revealed an overall positive feedback towards the application although the hardware was considered uncomfortable and too large. We conclude that the approach proved feasible and the acceptability was overall high, although advances in hardware and the patient-interface are necessary to assist patients suffering from Alzheimer's disease in daily activities.

3.2.3 Author´s contributions

The presented study was led by TUM (Chair of Human Movement Science) and performed in collaboration with Klinikum rechts der Isar (Department of Psychiatry/ Centre for Cognitive Disorders). Nina Rohrbach and Philipp Gulde share the first authorship of this manuscript and Nina Rohrbach is the corresponding author. All authors contributed to the final draft of the manuscript, read and approved the final manuscript.

Nina Rohrbach:	Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Visualization, Writing – Original draft, Funding acquisition
Philipp Gulde:	Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – Original draft, Visualization, Project administration
Alan Robert Armstrong:	Conceptualization, Methodology, Software, Funding acquisition
Linda Hartig:	Validation, Investigation
Anas Abdelrazeq:	Software, Data curation, Writing – Review & Editing, Funding acquisition
Stefan Schröder:	Software
Johanne Neuse:	Resources
Timo Grimmer:	Resources
Janine Diehl-Schmid:	Resources
Joachim Hermsdörfer:	Conceptualization, Methodology, Writing – Review & Editing, Supervision, Resources, Funding acquisition

3.2.4 Original publication II

Rohrbach *et al. Journal of NeuroEngineering and Rehabilitation* (2019) 16:66
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Journal of NeuroEngineering and Rehabilitation

RESEARCH Open Access

An augmented reality approach for ADL support in Alzheimer's disease: a crossover trial

Check for updates

Nina Rohrbach[1*†], Philipp Gulde[1†], Alan Robert Armstrong[1], Linda Hartig[1], Anas Abdelrazeq[2], Stefan Schröder[2], Johanne Neuse[3], Timo Grimmer[3], Janine Diehl-Schmid[3] and Joachim Hermsdörfer[1]

Abstract

Background: Dementia of the Alzheimer's type can impair the performance of activities of daily living and therefore severely impact independent living. Assistive technologies can support such patients when carrying out daily tasks.

Methods: In this crossover study, we used an augmented reality approach using a Microsoft HoloLens to support patients in a tea making task. During task execution, subjects received three-dimensional dynamic holograms of the sub-steps necessary to complete the task. Ten patients suffering from Alzheimer's disease were tested and post-hoc semi-structured interviews were conducted to assess usability.

Results: The patients committed errors when executing the task with and without holographic assistance. No differences in success rates or error frequencies were observed ($p_{success}$ = .250, p_{errors} = .887). Patients revealed prolonged trial durations (Glass' Δ = 1.475) when wearing the augmented reality headset. A model of multiple linear regression ($R^2_{adjusted}$ = .958) revealed an influence of the errors in the control condition and a moderation by the errors in the experimental condition. Patients with more severe problems in the natural performance of the task showed lower increases in trial durations when wearing the HoloLens.

Conclusions: We assume that the application was a secondary task requesting its own resources and impairing performance on its own. The regression suggests however that the given assistance was compensating these additional costs in patients with stronger needs of support. Interview data on usability revealed an overall positive feedback towards the application although the hardware was considered uncomfortable and too large. We conclude that the approach proved feasible and the acceptability was overall high, although advances in hardware and the patient-interface are necessary to assist patients suffering from Alzheimer's disease in daily activities.

Trial registration: DRKS, DRKS00014870. Registered 11 June 2018 - Retrospectively registered, TrialID = DRKS00014870.

Keywords: ADL, Augmented reality, Alzheimer's disease, Usability, Assistive technology, Mixed methods

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†Nina Rohrbach and Philipp Gulde contributed equally to this work.
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Background

Cognitive deterioration in patients with dementia, especially of the Alzheimer's type (AD), is known to negatively influence complex activities of daily living (ADL), such as shopping, navigating routines or preparing drinks and food [1–4]. Underlying factors can be loss of focus and memory function [5, 6] as well as signs of apraxia and action disorganization syndrome [7, 8]. The resulting ADL capacity can prohibit or limit independent living. So far, support is given by relatives and nursing services. The load and the cost of time and money are substantial for the patients and their relatives. While there is currently no cure for AD, a range of electronic devices to assist people with dementia has been developed [9, 10]. Augmented reality (AR) applications are a new possible approach to tackle these problems. AR can offer non-obtrusive guidance in everyday live.

Research shows that neurological patients are open-minded and have a positive attitude towards assistive technology to remain independent [11, 12]. The inclusion of the target group is thought to be crucial in the development process for the usability of the assistive technology end-product [12]. Usability can be defined as "the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use" [13]. In this crossover study, we examined the feasibility and usability of the AR approach using a head mounted Microsoft HoloLens (Microsoft Cooperation) to support patients with Alzheimer's disease in the execution of the ADL of tea making. Additional to performance parameters, we applied semi-structured interviews to involve the end users opinion.

Methods

Analytic approach

To examine the usability of AR guidance during the ADL of tea making in patients with AD, we applied a mixed method design [14] to obtain quantitatively abundant performance data by running a crossover study as well as the patients´ individual experiences conducting semi-structured interviews. Within the crossover study, the same ADL task (tea making) was performed in two conditions, one being the control condition (natural tea making), and the other being the experimental condition (AR-supported tea making). This design is useful because it allows a perfect match of subject characteristics as measurements of the same participants are compared. As our aim was to contextualize our quantitative findings using qualitative data, the reported results primarily stem from our quantitative data, but parallel data analysis helped to complement our findings [14].

Tea making task

The tea making task has been selected as an example of a relevant ADL task because it requires the ability to organize multi-step actions in a sequence of subtasks to achieve a goal, is highly relevant in many peoples life, and has been intensively studied in the literature in patients with brain damage, e.g. suffering from apraxia and action disorganization syndrome [15, 16].

Hardware

The Microsoft HoloLens (Microsoft Cooperation) head mounted display was chosen as a state of the art technology that would enable freedom of movement for users while still possessing the ability to deliver support through its built in mixed reality technology.

Software development

The AR application was developed within a user centered design approach consisting of four iterative cycles (March 2017 – December 2017) through collaboration between researchers, clinicians, patients and family members in the framework of the EU project "Therapy Lens" [17]. As recommended in the literature [12], testing in these predeployment phases took place in the patient's daily living environment outside the lab to better understand the needs and make participants feel more comfortable and part of the design process. The given feedback of different stakeholders [18, 19] resulted in the design of a step by step guidance system for a multi-step ADL task (tea making), incorporating audio-visual cues for each step, namely asking to:

1. Fill water into the kettle
2. Switch the kettle on
3. Add a tea bag to the mug
4. Wait for the water to boil
5. Pour the hot water into the mug
6. Remove the tea bag
7. Task is finished

Cues are given by a young female voice instructing the next step (including a displayed subtitle) and a holographic simulation of the corresponding step (Fig. 1).

Interactions are possible with the interface using three different control strategies, namely hand gestures, a clicker (similar to a computer mouse) or voice control. Given the novel nature of the device and the feedback during our development process, we decided to simplify the interaction to only one control strategy. The pilot interviews revealed a clear preference for speech recognition as the primary control strategy because of being the most intuitive allowing the hands free to interact [19]. Thus, after the completion of each step the patient proceeds to the next step by the voice

Fig. 1 Display of holographic cues presented by the Therapy Lens application on a Microsoft HoloLens. The subtitle and holograms indicate the first step in the tea making task of pouring the heated water into the mug ("Gieße das kochende Wasser in die Tasse"). The red kettle and the small white mug (on the right) are both holographic objects

command "weiter" (German for "next", recognized by a speech recognizer in the application). The application remains in the current step if the command ("weiter") is not given. The Therapy Lens application was developed in Unity 3D 2017.1.0 with the compatible HoloLens Tool Kit. The final demo of the used prototype was published and is freely available on the Microsoft Store since February 2018 under the name Therapy Lens [17].

Participants

This crossover study took place at the Center for Cognitive Disorders at the Department of Psychiatry and Cognitive Rehabilitation of the Klinkum rechts der Isar, Technical University of Munich in Germany, from January to March 2018. Participants were recruited, based on the following eligibility criteria: adult patients with diagnosed dementia of the Alzheimer's type, a normal or corrected-to-normal vision, and sufficient cognitive ability to understand and follow the task instructions. The sample consisted of 10 patients (71.8 ± 11.1a; 7 male, 3 female) suffering from mild and moderate dementia of the Alzheimer's type (Table 1).

Ethical considerations

Ethical approval in accordance to the declaration of Helsinki was obtained from the Ethics Committee of the Medical Faculty of the Technical University of Munich (reference number 175/17 S). All participants gave written informed consent.

Usability testing

Testing included the preparation of a hot cup of tea. Tea making was carried out twice for each of the conditions. These were the natural condition (control condition) and trials guided by an augmented reality application (Therapy Lens condition) for the Microsoft HoloLens. The first trial in both conditions was always a familiarization trial and not scored. Based on our experiences made in the previous developmental stages, we put emphasis on the correct fitting of the glasses as people who never experienced the HoloLens before tend to need more time for proper adjustment. As we were interested in the intuitive handling of the application's current form, the orientation with the device and its usage focused on a brief introduction to its basic functioning and control via voice command. In the natural condition patients were asked to prepare a cup of tea in a natural way, as if they were at home, with no emphasis on speed or accuracy, while in the guided condition patients were asked to follow the instructions given by the system step by step. Prior to all trials a DIN A4 picture of the end product (hot cup of tea) was shown to the

Table 1 Details of the patient sample

Patient	Age [1a]	Sex	Diagnosis (ICD)	Education	MMSE	Order of conditions
01	64	M	F00, F32.0	Diploma	22	C-T
02	69	F	F00	Doctor	19	T-C
03	51	M	F00, F32.0	Diploma	27	C-T
04	78	F	F00, F32.0	School	24	C-T
05	84	M	F00	Diploma	18	C-T
06	81	M	F00	Apprenticeship	25	C-T
07	57	M	F00	Apprenticeship	21	T-C
08	80	M	F00	Apprenticeship	27	C-T
09	77	F	F00, F32.0	Apprenticeship	25	T-C
10	77	M	F00	Apprenticeship	19	T-C
n = 10	*71.8, ±11.1*	*7x male, 3x female*	*10x AD, 4x depression*	*1x doctor, 3x diploma, 5x apprenticeship, 1x school*	*22.7 ±3.4*	*5x C-T, 5x T-C*

Legends: M male, F female, ICD international classification of diseases, AD Alzheimer's disease, MMSE Mini Mental State Examination, C-T control – Therapy Lens, T-C Therapy Lens - control; F00 Dementia of the Alzheimer's type; F32.0 mild depression patients (Fig. 2). The assignment to the orders of conditions were pseudo-randomly set prior to the first patient contact. Blinding of patients or researchers was not possible due to the device being used (AR glasses). The usability of the system was further assessed by video observations of dementia patients using the AR application and the conduction of semi-structured interviews.

Performance analysis

Used parameters for the performance analysis were the **trial durations** for the second trial of each condition (inactive waiting time for the water to boil was excluded), the **relative difference between the trial durations** of successful control and Therapy Lens trials, the **success** of achieving the task goal (hot cup of tea), the **age**, the **order of conditions**, and the **MMSE score**. Trial duration has been shown to be a valid marker of performance in the chosen task [4].

$$relative\ difference = \frac{Therapy\,Lens_{trial\ duration} - Control_{trial\ duration}}{Control_{trial\ duration}} \tag{1}$$

Further, an error analysis, based on video recordings was performed and **errors** were assigned to one of three error categories, namely: spatio-temporal, conceptual, and sequential [15]. Commonly observed ADL difficulties, as errors in the execution of the task (e.g. dropping an item) or the mislocation of an object (e.g. pouring water onto the table rather than into the glass) are scored as spatio-temporal errors. An example for a typical conceptual error is an action that is carried out, but not in an appropriate way (e.g. failing to open the kettle). Often observed sequencing errors include behaviors like performing an action much later than usual (e.g. switching the kettle on after preparing the cup of tea) or unintentionally omitting a step (e.g. turning the kettle on without having inserted water) [15].

Fig. 2 Picture of the end product (hot cup of tea) shown to all patients prior to each trial. Objects from left to right: Kettle, tea bags on a saucer, spoon, mug, saucer for used tea bags, and water container (filled with 500ml of room temperature water at the start of each trial)

Statistical analysis

The statistical analyses of the performance data included a McNemar test for paired samples to compare the number of successful trials between the conditions (control and Therapy Lens). For the parametric tests, only trial durations of pairs of successful trials were used for the analyses. Further, a Shapiro-Wilk test was applied to test for normal distribution of the trial durations. Then a repeated measures ANOVA was computed to compare the trial durations of both conditions. Finally, a repeated measures ANOVA with the between-subject factor order of conditions and the covariates age and MMSE score was used to compare the trial durations with respect to effects of order, age, or mental capacity. Additionally, a multiple linear regression (MLR) was run to model the relative differences in trial durations of successful trial pairs based the error metrics, age, MMSE, and the order of conditions. Effect sizes were Glass' Δ for the condition comparison. Variance inflation factor was set to < 5.00. α was set to .05.

Qualitative content analysis

The interviews lasted approximately 15 min, and were held in German language. They were based on an interview guide that consisted of general open questions regarding patients' experiences with the AR system and specific open questions on satisfaction with the hardware and the multi-dimensional support given by the system (Table 2). Interviews were audio recorded, transcribed word-for-word according to specified guidelines [20] using the software f4/f5transkript (dr. dressing & pehl GmbH) and pseudonymized. Interview data were analyzed using the structuring qualitative content analysis described by Kuckartz [20]. Main categories were formed a priori based on the lead questions and the literature [12] (Table 2).

Table 2 Three major codes affecting the usability

Code	Definition	Examples
Hardware	Hardware related factors influencing the user-friendliness and satisfaction	• Wearing comfort & design • Estimated duration of daily use
Software	Software related aspects influencing the user-friendliness and satisfaction	• Layout & design of cues • Structure • Functioning (command)
Acceptability	Reactions and emotions to the system Factors affecting the willingness to use the system	• Meaningfulness • Capabilities & Control • Effect of novelty

The interview data were coded and analyzed using the software MAXQDA Analytics Pro 2018 (Release 18.0.0, VERBI GmbH) by one person (NR). Based on systematically prepared thematic summaries, common themes were extracted, analyzed, and the meanings discussed with a second researcher (LH). Three major categories describing the usability of the AR application are presented in Table 2. The code "hardware" was assigned when device related barriers or facilitators were highlighted to affect the systems usability, e.g., the general wearing comfort and design of the hardware or the estimated acceptable duration to wear it during the day. The code "software" captured software related aspects influencing the usability, e.g., the design and the structure of the different presented cues or the reliability of the technology. The code "acceptability" served to capture the user's reactions to the system, i.e., emotions, and the acceptability based on a patient's capability to understand and use it. It includes factors affecting their willingness to use the system, e.g., the lack of a consumer's perceived benefit from using the system (meaningfulness), or positive and negative effects of a novel and unknown technology.

Results

Performance analysis

The average time to successfully perform the task was 77.14 s ±23.15 s in the control condition and 111.29s ± 24.10 s in the Therapy Lens condition (Table 3, Figs. 3 & 4). In the Therapy Lens condition three patients (P03, P05, P07) failed to successfully execute the task, while all patients were able to achieve the goal in the control condition (not statistically different, McNemar $p = .250$). The trial durations in both conditions were normal distributed (Shapiro-Wilk Control: $p = .267$, Therapy Lens: $p = .955$). A repeated measures ANOVA revealed a significant difference in trial durations between the conditions ($p = .017$, partial $Eta^2 = .638$, Glass' $\Delta = 1.475$). When including the order of conditions as a between-subject factor and age and MMSE as covariates, the resulting repeated measure ANOVA showed no effect of condition ($p = .199$), any interaction, or significance for the order of conditions ($p = .617$), the age ($p = .691$), and the MMSE score ($p = .867$).

The error analyses showed no significant differences for neither the summed up errors ($p = .887$) or the different error categories (conceptual: $p = 1.000$, sequential: $p = .078$, spatio-temporal: $p = .356$) (Table 3, Figs. 5 & 6).

Multiple linear regression revealed an impact of the summed up errors in the control condition, moderated by the summed up errors in the Therapy Lens condition (interaction term). The resulting $R^2_{adjusted}$ was .958 ($p < .01$). The β-weights were $Errors_{control} = -.858$ ($p < .01$) and interaction term $Errors_{control}$ x $Errors_{Therapy\ Lens} = -.361$ ($p = .01$). The moderation reduced the β-weight of $Errors_{control}$ from −.919 to −.858. All means and standard deviations are shown in Table 3. The results of the MLR are displayed in Fig. 7.

$$\begin{aligned} &predicted\ relative\ difference \\ &\quad = 1.023 - .264 * Errors_{control} \\ &\qquad - .052 * Interaction\ Term_{Errors\ Therapy\ Lens\ x\ control} \end{aligned} \tag{2}$$

Unsuccessful trials

Three patients failed to successfully use the Therapy Lens application, ergo were not able to achieve the task goal (hot cup of tea). Video analyses revealed that one patient (P05) failed to proceed further than step 1 ("Fill water into the kettle"), due to the inability to open the kettle's lid. Two patients (P03, P07) did not proceed beyond the second step ("Switch the kettle on"). One patient (P07) first tried to use the switch to open the kettle and therefore switched the kettle off after closing the lid. The other patient (P03) removed the kettle from its base when filling in the water and did not place it back on the basis (precluding power supply). Thus, in both cases the water did not start boiling and step 4 ("Wait for the water to boil") was therefore not achieved.

Interview data

The analysis of the semi-structured interviews revealed a range of opinions on the presented ADL support system. We identified three major categories from the content analysis of the interview data affecting the usability of the system: hardware and software related issues and the acceptability (Table 2).

Table 3 Means, standard deviations, significance levels, effect sizes for the used parameters in the two conditions Therapy Lens and control

	Trial durations†	Relative difference†	Successful/ failed trials	Summed errors†	Conceptual errors†	Sequential errors†	Spatio-temporal errors†
Control condition	77.14 s	.53 ± .43	10/0	1.57	.71	.71	.14
	±23.15 s			±1.40	±1.11	±.49	±.38
Therapy Lens condition	111.29 s		7/3	1.43	.71	.29	.43
	±24.10s			±1.62	±.95	±.49	±.53
Significance	p = .017 Glass' Δ = 1.475	–	p = .250	p = .887	p = 1.000	p = .078	p = .356

Legends: *†Based on pairs of successful trials*

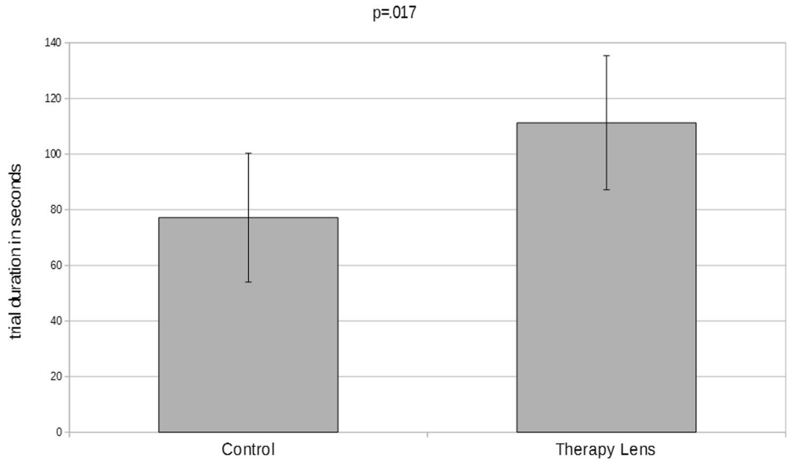

Fig. 3 Means and standard deviations of the trial durations in seconds for the two conditions: control and Therapy Lens

Hardware

According to the interviews, most of the patients (70%) could imagine to wear the AR headset between 15 and 60 min a day before they would need a break, with a maximal mentioned duration from "less than one minute" (10%; P05) to "up to several hours including breaks" (20%; P06, P10). The core aspect criticized by the patients referred to the hardware related wearing comfort. While two participants valued the device as relatively light weighted (20%), six participants (60%) criticized it by describing it as: "too big", "bulky", "impractical", "heavy", "obstructive", or "monstrous", which was influencing the extent to which the application would be used, as communicated by one patient (P04):

> "I liked it, but I do not want to wear it. […] Because that would bother me, because it's just such a big thing. […] It's great, but I do not want it (laughs). It's great because you can read it nicely in there. It is very clear, you can read it clearly, clearly big. […] But that's such a big thing. It's just too big."

Software

The majority of examined patients (90%) was able to control the system using the required voice command "weiter". 40% of patients highlighted the well reacting speech function. However, patients occasionally needed extended periods of time to remember the correct command, or, in other cases, patients automatically carried

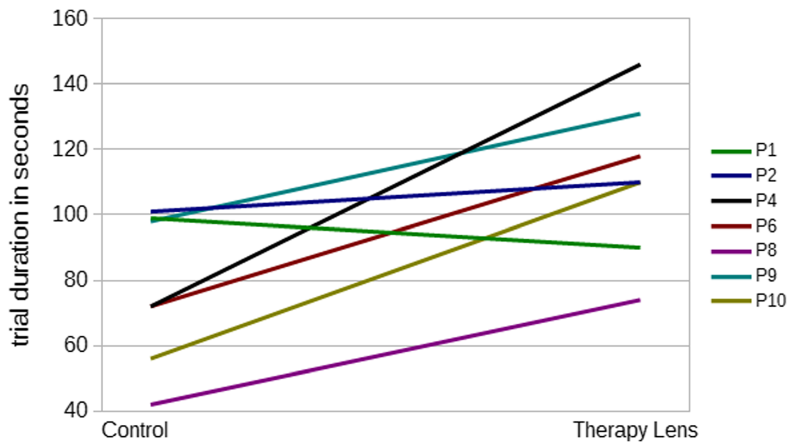

Fig. 4 Change of trial durations between the control and the Therapy Lens condition for the seven patients with successful trials in both conditions

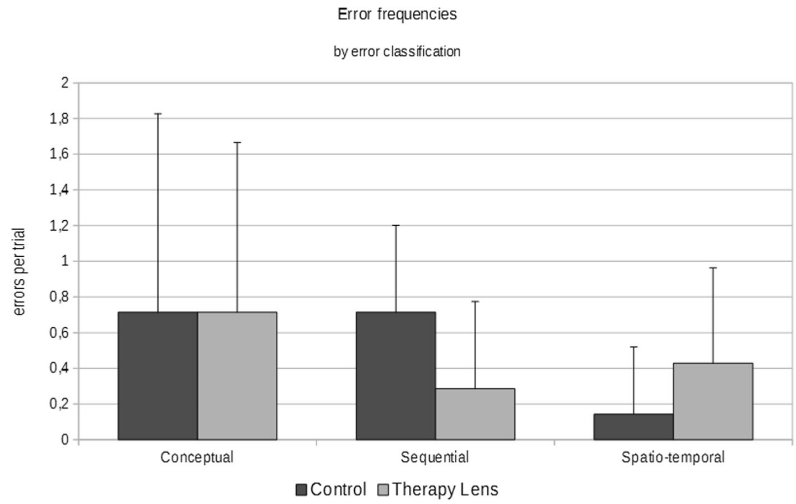

Fig. 5 Error frequencies by error classification in the control and Therapy Lens condition in successful trials

out the task without making use of the speech command or were passively waiting for more instructions after a step was finished. Thus, the fixed sequence of actions (step 1–7) was confusing for some participants who only used it partially. For instance, P03 proceeded with step 3 ("Add a tea bag to the mug") before giving the speech command to trigger this specific step. The patient was asking for more information and feedback, e.g., about the total amount of steps needed to fulfill the task. At the end, the patient failed to execute the task due to the inability to boil the water. The patient expressed the situation as follows (P03):

> "Then the waiting until the next step [...] and then the question how long does it take? [...] And then wait until someone says it is enough? Or does it proceed on its own? [...] When is this stupid thing (kettle) finally boiling or will there come several steps [...] and one step with the tea bag was not right. First came ... , that was reversed, I think, there was somehow a reversal of the order."

The opinion on the multi-dimensional cues (audio, subtitle, and holograms) differed between participants. While some recommended keeping text information because of

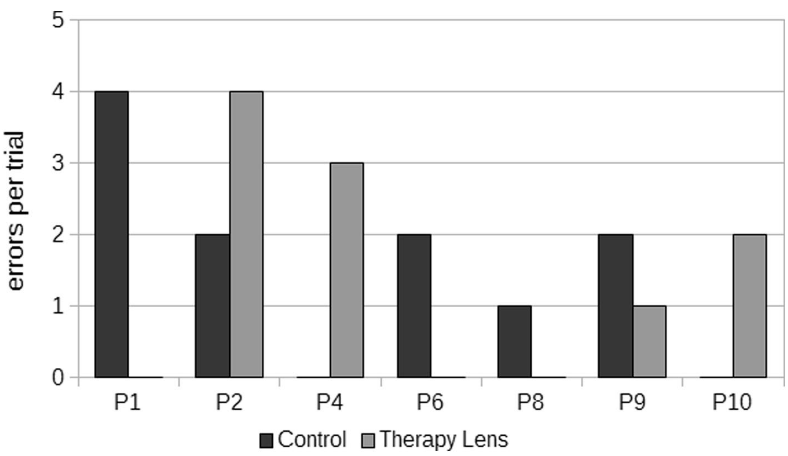

Fig. 6 Error occurrences in the control and the Therapy Lens condition for the seven patients with successful trials in both conditions

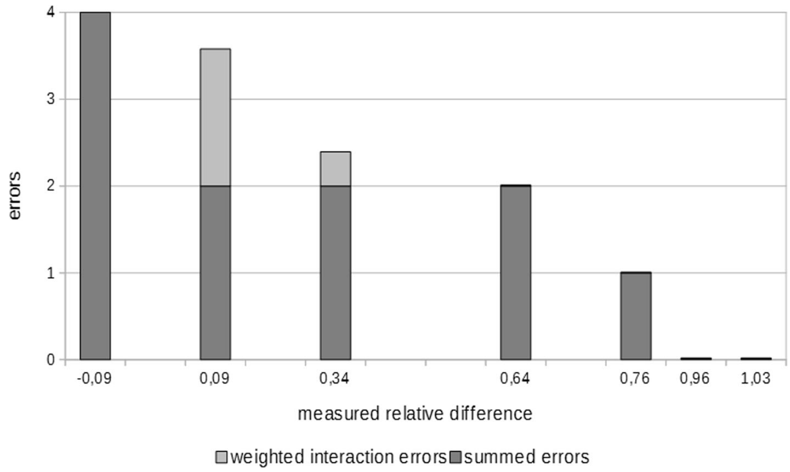

Fig. 7 Association of measured relative difference and error according to the model of multiple linear regression ($R^2_{adjusted}$ = .958, $p < .01$). The interaction errors (control condition x Therapy Lens condition) are weighted based on the model's coefficients. Each bar represents one of the patients

potential hearing problems (40%), others were in favor of audio support due to potential visual impairments (50%). Two patients positively mentioned the "clear readability" and the "pleasant voice" (20%). Most patients seemed to appreciate the combination of several dimensions to "avoid misunderstandings" (P09). 40% of patients were highlighting the holographic animations because of being "easier to store" (P01). One patient emphasized (P03):

> "[…] But a picture is worth a thousand words. This is already clear."

No negative opinion was given towards the holographic animations, but two patients were not able to remember them at all (20%; P05, P08).

Acceptability

The users judged their experiences differently. One patient described the experience as unusual and very new, since the patient has never used such a device before, and that there was a need for more time and interaction to orientate and to build an opinion on whether it is useful for the patient or others (P07). In another case, the cueing system caught a patient's attention who described it as (P09):

> "[…] very interesting […], so I became curious."

While some patients stated an added value for daily task support, e.g., one saying that with the help of the AR support the patient "would not forget anything" (P04), there were others who were not willing to use the application (P05), did not fully understand the concept (P02), or were questioning the application because of not seeing its meaningfulness due denying their diagnosis or need for support (P09):

> "I do not think I need help at home."

Discussion

In this study we introduced an augmented reality application via a headset to patients with Alzheimer's disease in order to support them during the performance of the activity of daily living of making a cup of tea. Our analyses revealed that the introduction of the Therapy Lens application had no clear positive effect on the patients' performance. Errors during task execution did not change significantly, although a trend (p = 0.078) towards less sequencing errors in TL could be observed (Table 3, Fig. 5). Further, the duration of task execution actually increased in TL (Table 3, Figs. 4 & 5). We could not find influences of the order of conditions, the age, or the MMSE score on the prolonged trial duration. Apparently, neither the age nor the mental capacity are good predictors, if and to what degree the application of Therapy Lens is detrimental. Data from semi-structured interviews on the usability of the AR headset revealed an overall positive experience, although the hardware was still considered as uncomfortable and too large (e.g., "bulky"). Even though the reliability of answers of AD patients is sometimes questionable [21], made observations and the patients' opinion in this study allow us to gain a better understanding in how AR applications can assist daily life activities in AD patients.

In the control condition participants were asked to perform the task of making a cup of tea in a natural way, without emphasis on speed or accuracy. From a qualitative perspective (see Software), we assume the longer trial durations in the Therapy Lens condition to be partially based on the following factors:

1. Patients were following a predefined order of steps not allowing for a simultaneous execution of steps.
2. Patients awaiting and perceiving the cues before performing the current step and pausing after the execution of a step and awaiting further feedback or instruction.
3. Patients not immediately remembering the appropriate voice command.

Quantitative data allowed modeling of the relative differences of trial durations between the two conditions. The resulting MLR revealed that increments of trial durations in the Therapy Lens condition were strongly dependent on the performance, in terms of errors, in the control condition, whereat increased error occurrences where associated with smaller relative differences. This was moderated by the error frequencies in the Therapy Lens condition. Taken together, the less support would have been needed in the control condition the worse was the application of the Therapy Lens for the ADL performance in terms of duration. This was to a small part caused by problems interacting with the augmented reality headset ($\beta\Delta$ $\text{Errors}_{\text{control}}$ = .061), but mainly by the burden of a secondary task being partially compensated by the support of the application in patients with ADL impairments.

The acceptance of assistive technologies is expected to vary during the course of dementia, i.e., acceptance can improve when symptoms start to threaten the independence of the patient [12]. Having this in mind and supported by the MLR, we suggest that the presented “step by step” approach may be most beneficial for more severe affected patients. However, when targeting this patient group one has to consider the possible resistance by the users when denying their diagnosis, as often observed in people with dementia [12] and depicted by our qualitative data (see Acceptability). For instance, one of the patients (P05) had a very strong reluctance in accepting the AR approach, stating that he does not want to use it. He also failed to complete the task in the AR condition because of not being able to open the lid of the kettle even though he managed this step before in the natural condition. His denial might have negatively influenced his performance.

Another important aspect to consider is that neurodegenerative changes caused by dementia can even make using mainstream devices problematic for some people with dementia. Further, the reduced ability for new learning in dementia patients may impact actual usage of a novel technology [12]. Herein, we confronted patients with a new technology that we introduced only by a short familiarization trial. The AR application required higher cognitive demands when processing the augmented cues and controlling the new device while performing a complex multi-step task. While we tried to keep the handling of the device as simple as possible by using speech control that requires only one word, both, the application of the command and the integration of the predefined “step by step” guidance into an often performed task appeared challenging for patients. This could potentially be compensated for by a longer familiarization period or practice sessions. Additional feedback given by the system, e.g. a holographic timer providing information on the brewing time as demanded by one patient (P03) or a reminder function after a certain time of pausing in the case a patient is losing focus, might potentially also support usage.

Including participants early in the development of assistive technology is recommended [12]. Indeed, when qualitatively reviewing the video recordings and analyzing the interview data, it became obvious that reasons for failure or longer trial durations seemed to be largely due to a lack of intuitiveness. The experienced malfunctioning of a technical device is potentially frustrating the user, thus, influencing the willingness to use the application. Consequently, to enhance the final acceptance of such an application it is vital to integrate the users’ feedback into future development. Apparently, as soon as technical support is given, users trust the system’s instructions with the given risk of over-reliance. In the tested system, the implemented number of seven steps was insufficient as patients got confused due to missing details. For instance, another reason why one of the patients (P03) failed in the AR condition was due to a missing cue between the first and the second step (i.e. placing the kettle to its base after filling in the water to allow boiling). Even though he was wondering why the kettle was not starting to boil the water, he was not able to solve the problem himself, but relying on the given instructions instead. We therefore suggest increasing the amount of support by integrating a higher quantity and more detailed steps (i.e. opening and closing the lid of the kettle) to allow for unrestrictive and straightforward guidance. Besides the mentioned discomfort related to the uncomfortable and large hardware, we did not observe any adverse events; like motion sickness or headaches.

Addressing the heterogeneous needs of persons with dementia is a well-known challenge [12]. Based on our study, patients value the integration of multiple cues (audio, text, holograms). The potential of holographic animations to support ADL tasks was supported by patients stating that their attention was caught and their interest awakened. However, not all patients noticed or remembered the holograms. We hypothesize that the simultaneous presentation of multiple cues was overwhelming, thus some information was masked out. In future trials, different cues (e.g., number and mode of presentation) should be evaluated against each other to investigate the most beneficial way of augmenting feedback to the real world environment in people with limited cognitive performance, although the used multi-modal approach ensured reliable cueing when dealing with comorbidities like partial loss of vision or hearing problems.

Conclusions

In conclusion, the prolonged duration of the experimental condition may be interpreted as an indicator of impaired performance of the ADL task, as a result of dealing with a secondary task (AR application). So far, the constraints, i.e., the unnatural interaction with the application and a drag of attention to the holograms from the real objects, preponderate the support in sequencing the task to a goal directed order of steps. Still, MLR revealed that in patients with more severely impaired performance dual task costs due to the application were almost balanced by the given support. Overall, the acceptability of the AR application appeared to be high, as a large part of participants revealed a positive attitude towards the system, although the hardware was considered the main impediment. This leads us to the conclusion that the paradigm of augmented support is generally working, but the implementation still needs an improved user-interface. Future hardware advances in AR will allow such applications to significantly assist patients with ADL impairments and promote independent living. The aim of the study was to test for usability and feasibility but also to provide directions for further improvements. To increase intuitiveness of our system, the next step will be to incorporate the obtained feedback in our future adjustments, followed by a postdeployment stage in close partnership with all potential end users, including clinicians and carers. Specifically, we will focus on the 1) optimization of cues by increasing the amount and details of the steps; 2) promotion of familiarization by incorporating a longer practice session; and 3) personalization by allowing the user to decide on the type of feedback (holographic animations and/or audio and/or text).

Abbreviations

AD: Alzheimer's disease; ADL: Activity/ies of daily living; AR: Augmented reality; C-T: Order of conditions: Control condition first; F / M: Female / Male; MLR: Model of multiple linear regression; MMSE: Mini Mental State Examination; T-C: Order of conditions: Therapy Lens condition first

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Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author [NR]. The data are not publicly available due to containing information that compromise research participant privacy/consent.

Authors' contributions

PG, NR, and JH designed the study. JN, TG, and JD-S diagnosed and selected the patients. AA, SS, ARA, and NR developed the AR application. PG and LH performed the lab testing. NR and LH analyzed the interview data. PG and LH assessed and scored the ADL performance. PG performed the statistical analyses. All authors contributed to the final draft of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval for the study was given by the Ethics Committee of the Medical Faculty of the Technical University of Munich (reference number 175/17 S). All participants gave written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests with regards to the submitted work. Outside the submitted work TG reported having received consulting fees from Actelion, Eli Lilly, Iqvia, Quintiles, MSC, Novartis, Roche Pharma, lecture fees from Biogen, Lilly, Parexel, Roche Pharma, and grants to his institution from Actelion and PreDemTech.

Publisher's Note

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3.3 Fooling the size-weight illusion – Using augmented reality to eliminate the effect of size on perceptions of heaviness and sensorimotor prediction

3.3.1 Visual abstract

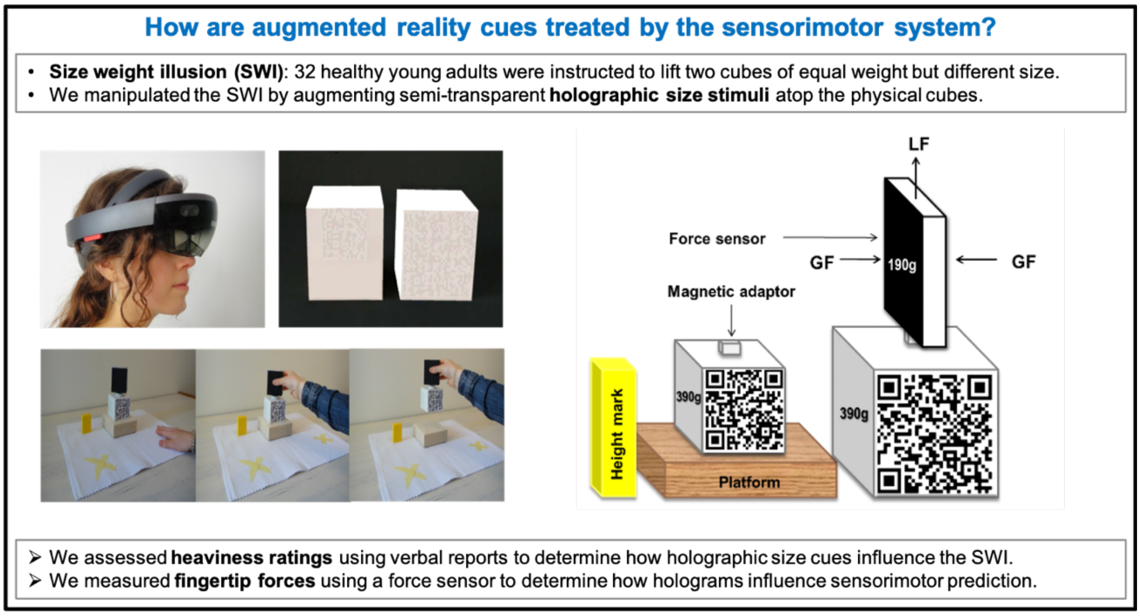

Figure 12. Visual abstract study III.

Authors: Nina Rohrbach, Joachim Hermsdörfer, Lisa-Marie Huber, Annika Thiefelder and Gavin Buckingham

Title: Fooling the size–weight illusion—Using augmented reality to eliminate the effect of size on perceptions of heaviness and sensorimotor prediction.

Journal: Virtual Reality

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Data/code: All project files are publicly available at the Open Science Framework website: https://osf.io/fz368/. The full project code is available on GitHub https://github.com/athierfelder/size-weight-illusion.

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3.3.2 Summary

Augmented reality, whereby computer-generated images are overlaid onto the physical environment, is becoming significant part of the world of education and training. Little is known, however, about how these external images are treated by the sensorimotor system of the user – are they fully integrated into the external environmental cues, or largely ignored by low-level perceptual and motor processes? Here, we examined this question in the context of the size–weight illusion (SWI). Thirty- two participants repeatedly lifted and reported the heaviness of two cubes of unequal volume but equal mass in alternation. Half of the participants saw semi-transparent equally sized holographic cubes superimposed onto the physical cubes through a head-mounted display. Fingertip force rates were measured prior to lift-off to determine how the holograms influenced sensorimotor prediction, while verbal reports of heaviness after each lift indicated how the holographic size cues influenced the SWI. As expected, participants who lifted without augmented visual cues lifted the large object at a higher rate of force than the small object on early lifts and experienced a robust SWI across all trials. In contrast, participants who lifted the (apparently equal-sized) augmented cubes used similar force rates for each object. Furthermore, they experienced no SWI during the first lifts of the objects, with a SWI developing over repeated trials. These results indicate that holographic cues initially dominate physical cues and cognitive knowledge, but are dismissed when conflicting with cues from other senses.

3.3.3 Author´s contributions

Nina Rohrbach is the first author and corresponding author of this manuscript. All authors contributed to the final draft of the manuscript, read and approved the final manuscript.

Nina Rohrbach:	Conceptualization, Methodology, Software, Data curation, Writing – Original Draft, Visualization, Project administration, Funding acquisition
Joachim Hermsdörfer:	Conceptualization, Methodology, Formal analysis, Resources, Writing – Original Draft, Visualization, Supervision, Funding acquisition
Lisa-Marie Huber:	Formal analysis, Investigation
Annika Thierfelder:	Software
Gavin Buckingham:	Formal analysis, Writing – Review & Editing

3.3.4 Original publication III

Virtual Reality
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ORIGINAL ARTICLE

Fooling the size–weight illusion—Using augmented reality to eliminate the effect of size on perceptions of heaviness and sensorimotor prediction

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Abstract
Augmented reality, whereby computer-generated images are overlaid onto the physical environment, is becoming significant part of the world of education and training. Little is known, however, about how these external images are treated by the sensorimotor system of the user – are they fully integrated into the external environmental cues, or largely ignored by low-level perceptual and motor processes? Here, we examined this question in the context of the size–weight illusion (SWI). Thirty-two participants repeatedly lifted and reported the heaviness of two cubes of unequal volume but equal mass in alternation. Half of the participants saw semi-transparent equally sized holographic cubes superimposed onto the physical cubes through a head-mounted display. Fingertip force rates were measured prior to lift-off to determine how the holograms influenced sensorimotor prediction, while verbal reports of heaviness after each lift indicated how the holographic size cues influenced the SWI. As expected, participants who lifted without augmented visual cues lifted the large object at a higher rate of force than the small object on early lifts and experienced a robust SWI across all trials. In contrast, participants who lifted the (apparently equal-sized) augmented cubes used similar force rates for each object. Furthermore, they experienced no SWI during the first lifts of the objects, with a SWI developing over repeated trials. These results indicate that holographic cues initially dominate physical cues and cognitive knowledge, but are dismissed when conflicting with cues from other senses.

Keywords Weight illusions · Perception · Sensorimotor control · Virtual reality · Holograms

1 Introduction

Immersive virtual reality (iVR) typically involves allowing an individual to experience, and interact with, a computer-generated environment as if it were the physical environment. Recent technological advances and cost reductions have significantly widened access to this technology, which has become a significant part of the consumer entertainment industry and its potential is rapidly being seen as a training aid for medical education and dangerous industries (Allcoat and Mühlenen 2018; Bideau et al. 2010; Rohrbach et al. 2019a). A less widespread technology, which has arguably more potential for broad integration into society, is augmented reality (AR). AR systems use either a camera or a transparent screen to provide a live view of the physical environment overlaid with computer-generated images to augment the viewer's perspective of what they are viewing. In its simplest form, a smartphone with a camera is capable of delivering a reasonably compelling AR experience. More sophisticated devices, such as the Microsoft HoloLens, use translucent lenses, external sensors, and holographic projection to overlay individual graphical elements to discrete elements of the physical environment. This technology, while far from widespread, has significant potential to fundamentally alter real-time access to information in the classroom and the workplace (Dey et al. 2018) and has recently been trialled as a way to support clinical populations (Rohrbach et al. 2019b). Further, AR provides a better sense of presence than VR because the user can see their own body parts interacting with the real environment (Al-Issa et al. 2012). Little is known, however, about how the perceptual system

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of the user treats computer-generated virtual cues, nor about how this virtual information interacts with the sensory input from objects in the physical environment.

The objective of this experiment was to determine whether the size–weight illusion (SWI) can be manipulated by augmenting the apparent size of the stimuli with holographic size stimuli. The SWI describes the experience that small objects feel heavier than equally weighted larger objects (Buckingham 2014; Charpentier 1891). Although the precise mechanisms underpinning this effect are still robustly debated (Dijker 2014; Freeman et al. 2019; Peters et al. 2016; Plaisier et al. 2019), the magnitude of the illusion (i.e. how much heavier the small object feels relative to the large object) appears to relate to expectations of heaviness elicited by the apparent volume of the stimuli (Buckingham and Goodale 2013; Buckingham and MacDonald 2016). Indeed, the magnitude of the illusion appears to be related to the reliability of the cue though which object volume is experienced. For example, a recent study has shown that impairing vision with specially designed goggles reduced the degree to which a small set of objects felt heavier than a larger set (Wolf et al. 2018). If one's 'belief' in the size information they are experiencing is a mitigating factor in the SWI, it seems plausible that this effect can be used to provide an insight into how the perceptual system treats novel cues. This has been shown, for example, in the case of human echolocation, whereby unsighted individuals can gain knowledge of their surroundings by interpreting the echoes returned from self-generated vocalizations or clicks. Buckingham et al. (2015) showed that blind echolocators had their experience of object weight affected by the size cues induced by these echoes, which provided new insights into the degree this substituted sense was a genuine replacement for vision.

In the context of augmented reality, the SWI could thus become a proxy to determine how our perceptual systems value AR cues in relation to those generated by the physical environment. It is increasingly well-established that altering visual gain (i.e. increasing of decreasing the speed of the computer-generated object compared to its physical counterpart) can alter the experience of object weight (Von Polanen et al. 2019; Weser and Proffitt 2019). Several studies have already used the SWI in the context of immersive virtual reality through a stereoscopic head-mounted display to show that virtual size cues are capable of affecting how heavy an object feels when lifted (Buckingham 2019; Heineken and Schulte 2007; Kawai et al. 2007). Furthermore, a recent compelling study from van Polanen and Davare (2019) showed that altering the sizes of objects while they are being lifted in a VR environment affects their weight. Interestingly, all of these studies note that visual cues to size delivered through computer-generated images in VR yield a smaller illusion than is experienced when the size cues are experienced through cues from the physical environment. While this might suggest that we prioritize cues derived from the physical environment over computer-generated equivalents, this supposition has never been directly tested. The semi-translucent computer-generated images which are overlaid on the cues from the physical environment in AR provides a unique opportunity to directly examine how these distinct sources of information interact within a single modality.

In addition to examining how augmented reality might affect the experience of object weight, this paradigm also allows us to examine how these computer-generated cues might affect the fingertip forces used to grip and lift objects. Skilful object manipulation requires the application of appropriate forces. A lifter's expectation of object heaviness influences the nature of this interaction, such that the peak values of grip and load force rates which occur prior or at the time of lift-off serve as a measure for sensorimotor prediction (Li et al. 2011). In the physical environment, a plethora of studies have shown that fingertip force rates (i.e. the maximum of first derivative of a grip force signal or the weight change, respectively) reflect the apparent weight (as signalled by the size) of objects during the initial lifts of objects (Gordon et al. 1991; Nowak and Hermsdoerfer 2009). This reliance of visual expectations from prior experience means that, in a typical SWI paradigm, the large object is gripped and lifted at a higher rate of force than the small object on the first pair of lifts (Buckingham et al. 2011; Davis and Roberts 1976). These long-term expectations are quickly discarded in favour of more short-term evidence based on tactile and visual feedback from the lifts themselves, meaning participants adapt their fingertip force rates to the actual (and thus identical) masses of each object (Flanagan and Beltzner 2000; Grandy and Westwood 2006). In an unpublished Masters thesis, Metcalfe (2007) compared a traditional SWI to a visuo-haptic SWI created in an augmented environment. Despite a lack of vision of the grasping hand and the physical cubes in the augmented environment, participants judged the cubes to feel similarly heavy. The study reaffirmed the robustness of the SWI in both environments. However, despite the persisting perceptual illusion, a steady difference in kinematics between cubes that changed in the same way for all cube sizes was reported. It was suggested that visual and haptic size cues can override sensorimotor memory and that AR is suitable in simulating the natural environment. To our knowledge, neither the initial parameterization of fingertip force rates, nor the subsequent adaptation processes, have been examined in the context of virtual or augmented reality–it is unknown whether the sensorimotor system will respond to computer-generated and augmented environments in a way which reflects performance in the physical environment, which has obvious consequences for the wider uptake of AR in society.

Here, we tested whether computer-generated size cues delivered with an AR system could override the properties of real-world objects. Participants in one group lifted SWI-inducing objects, reporting how heavy they felt after each lift and having their fingertip forces measured during each lift. Participants in another group lifted the same objects which had semi-transparent holograms of identically sized cubes overlaid atop the (still-visible) physical objects. If augmentation with virtual cues overrides with cues information from the real objects, the SWI will be eliminated and participants will experience the identically sized objects as having the same (true) mass. Furthermore, if holographic size cues are utilized by the sensorimotor system at the expense of the size cues from the physical environment, the objects should be gripped and lifted with similar rates of force.

2 Materials and methods

2.1 Participants

A total of 32 healthy young adults (20 women, 12 men), aged 23.6 years (SD = 3.1) took part in the experiment. Participants were recruited from Munich and tested in the native language (German) at the Human Movement Science lab at the Technical University of Munich, in Germany. Eligible subjects were (1) all adults aged 18 to 40 with (2) a normal or corrected-to-normal vision. Exclusion criteria were (1) a history of neurological diseases or (2) upper limb impairment. All but one person in the AR group was right-handed according the Edinburgh test (Oldfield 1971), ten subjects used their visual aids during the experiment (7 in the AR group). None of the participants reported any visual or sensorimotor problem. Nine subjects had previous VR experience (6 in the AR group) but none of them were familiar with the experimental task or the hypotheses being tested. All subjects included in this study gave written informed consent prior to testing. Ethical approval in accordance with the declaration of Helsinki was obtained from the Ethics Committee of the Medical Faculty of the Technical University of Munich (reference number 175/17 S). Participants were randomly assigned into the AR group or the Control group (Table 1).

2.2 Stimuli and equipment

Subjects were instructed to lift two white plastic cubes of equal weight (390 g) but different size (big cube 10.0 cm × 10.0 cm × 10.0 cm; small cube 6.3 cm × 6.3 cm × 6.3 cm). A metal insert was added to the geometric centre of the small cube to raise its weigh to that of the large cube. A magnetic adaptor mounted in the centre top of both cubes served as a removable connector with a 190 g handle that contained force sensors (Li et al. 2011) and facilitated quick exchange between the two cubes. Sandpaper was attached to the two vertical grasping surfaces to prevent slippage (Fig. 1a). The force sensors registered grip forces applied orthogonally to the grasping surfaces (MAK 177, range 0–100 N, accuracy ± 0.1 N, Rieger, Rheinmünster) as well as the load force acting tangentially to the surfaces along the vertical axis of the handle (MAK 177, range ± 50 N, ± 0.1 N). Signals were transmitted wirelessly to a PC with a sampling rate of 125 Hz.

The AR group wore a Microsoft HoloLens (1st generation) device, an optical-see-through system. When the user is looking through the glasses of the display, three-dimensional virtual cubes which matched the dimensions of the large cube (10.0 cm × 10.0 cm × 10.0 cm) appeared on the physical cubes (Fig. 1b). The small cube was placed on a wooden platform (10 cm x 10 cm × 3.7 cm) such that the top surface of the virtual and physical cubes was aligned (Fig. 1c). Exemplary videos demonstrating the experimental setup from the first-person perspective can be accessed via the Open Science Framework (OSF) https://osf.io/fz368/ (Rohrbach et al. 2020a).

Table 1 Comparison of the demographics between the AR and control groups

Group	N	Age in years (range)	Gender (m / f)	Handedness (r / l)
AR	16	23.6 (20–32)	10/6	15/1
Control	16	23.6 (20–29)	3/13	16/0

2.3 Augmented reality

For the AR group, the physical cubes were superimposed with slightly transparent cubic holograms. Holograms consist of light points that are projected into the user's field of view. In this article, a hologram refers to the perception of a computer-generated object through stereo imaging. The application for the experiment was developed in Unity 3D version 2017.4 (Unity Technologies 2019). Vuforia (Vuforia Engine 2018) was integrated into the Unity Framework and used to superimpose the virtual cube onto the physical cube. Vuforia offers several functionalities, including target tracking, i.e. the tracking of predefined images. An important aspect for our research question was to develop virtual objects that (1) convey the impression that they were present in the real environment and (2) still allow the subjects to easily see the physical cube. To do so, the holograms which were basic cube primitives, were adjusted in colour, structure, and brightness to create a strong contrast and to optimize the perception of the presented cubes being three-dimensional but also appeared

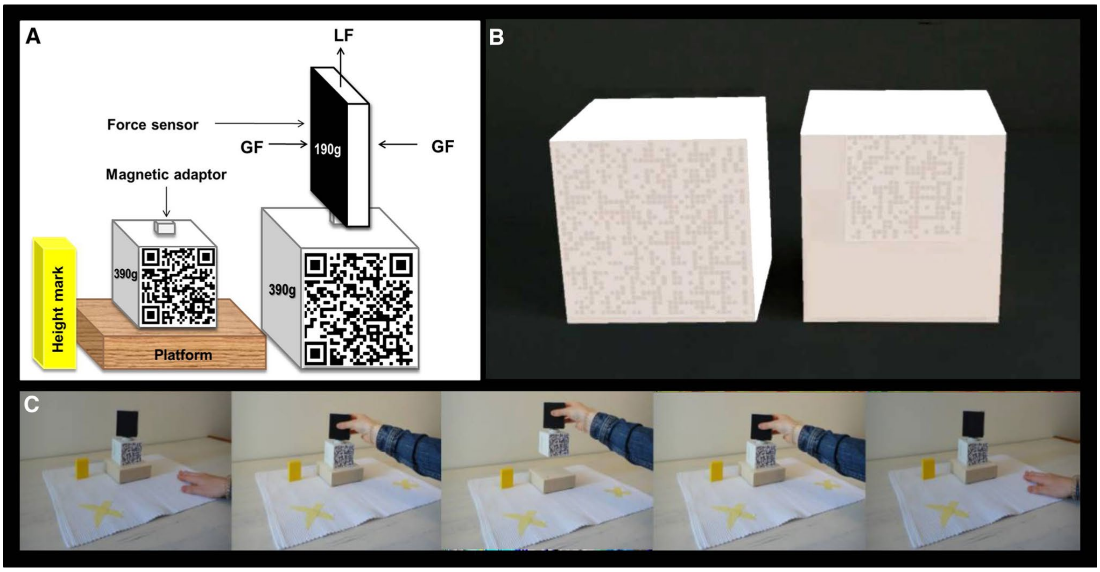


Fig. 1 **a** Schematic of the boxes which were lifted by participants, **b** the view from the participant's perspective in the AR condition, with the identically sized virtual boxes overlaid atop the physical boxes and **c** photographs of the task in action

slightly transparent to enable users to see through. Further, we wanted the virtual objects to remain overlaid atop the physical cube when being moved to increase the sense of presence. We therefore developed patterns, based on QR codes, which were attached to the physical cubes and loaded into the Unity project. This allowed us to precisely scale and align the holographic cubes relative to the cube throughout the experimental trials. The full project code is available at GitHub https://github.com/athierfelder/size-weight-illusion (Rohrbach et al. 2020b).

2.4 Study protocol

During testing, subjects were seated in front of a table and a white wall. First, participants were shown both cubes and asked to estimate the cubes' weights by verbally indicating a self-chosen number (pre-liftoff rating = T0). Note that participants of the AR group did not wear the HMD while giving these pre-liftoff ratings. This was the only moment the boxes were seen simultaneously by the subjects. Participants were then familiarized with the task with five lifting trials solely with the handle, followed by nine pairs of experimental lifts during which they lifted the cubes in alternation.

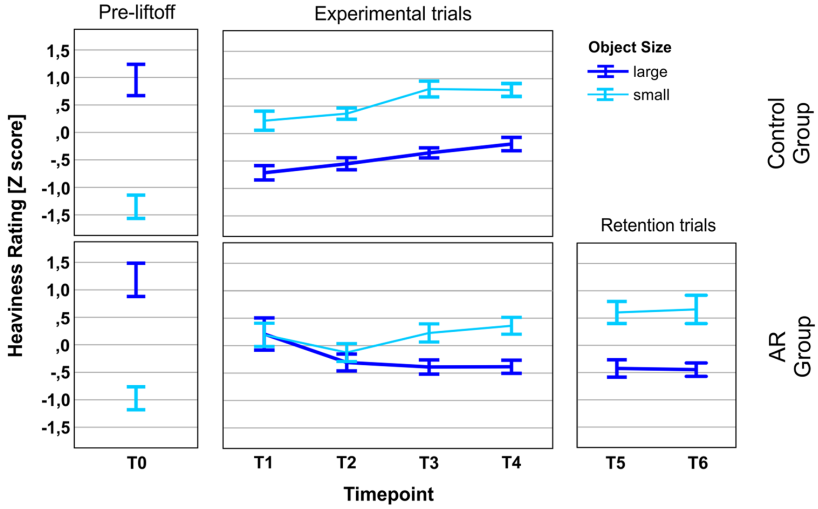
Prior to each trial, they were asked to close their eyes, at which point a single object was placed on the table in front of them. Following an acoustic signal, they were instructed to open their eyes and lift the cube with their dominant hand utilizing their thumb, middle, and index finger about up to 5 cm in a smooth and rapid way, hold it steady for 4 s until a second acoustic signal indicated to return back to the starting position. Between trials, while the cubes were exchanged, the subjects were first instructed to close their eyes, and then verbally informed about the actual size of the upcoming physical cube to be lifted (i.e. 'please lift the large/small box').

After the first and the second lifts of the experimental trials (first pair of lifts = T1) and, respectively, after the third (T2), sixth (T3), and ninth pair (T4) participants were again asked to report the felt weight in relation to the value given on the previous trial. Estimations were always given directly after one cube was lifted (i.e. small cube–weight estimation–large cube–weight estimation).

Participants in the AR group carried out a further three pairs of 'retention' lifts, where no augmented boxes were overlaid on the physical boxes, to determine whether any transient effects of AR remained after its removal. Heaviness ratings were further given after the first (T5) and third pair (T6) of these retention lifts. Lifting order was counterbalanced between subjects, and reversed every three pairs of lifts.

At the end of the lifting trials the intervention group was further asked to fill out a questionnaire measuring presence in AR environments (Regenbrecht and Schubert 2002) comprising seven questions that were answered on a 7-point Likert scale. It examines elements of realness (component 1, Q1-3), elements of spatial presence (component 2, Q4-5)

Fig. 2 Average normalized heaviness ratings for the pre-liftoff ratings (T0), the experimental trials (T1-4) and the retention trials (T5,6). Error bars indicate standard error of the mean. The dark blue (black) bars represent the large object and the light blue (grey) bars represent the small object. (Color figure online)



and elements of the experience of perceptual stress (component 3, Q6-7). The detailed questions are accessible via OSF https://osf.io/fz368/ (Rohrbach et al. 2020a).

2.5 Analysis

Numerical ratings of heaviness were standardized to a z-distribution based on the mean and standard deviation of an individual's ratings throughout the course of the experiment (T0 to T4). For the retention trials, which were only conducted in the AR group, means and standard deviation of T0 to T4 in this group were used to calculate the Z-scores of T5 and T6. These ratings were analysed with a mixed design 2 × 2x4 ANOVA with one between-group factor (group: AR, Control) and two within-subject factors (object size: large, small) and timepoint (T1, T2, T3, T4). The data from T5, T6 in the AR group were analysed with a separate within-subject 2 × 2 ANOVA with factors of object size (large, small) and timepoint (T5, T6). The pre-liftoff (T0) ratings were examined with a mixed 2 × 2 ANOVA with object size (large, small) as the within factor and group (AR, Control) as the between-group factor).

Customized software (GFWin, MedCom, Munich) collected and analysed the data. The grip force was averaged from the signals of the two grasping surfaces and the load force was normalized to a pre-liftoff baseline. The values were differentiated to yield their rates of change. The peak grip force rates (GFR) and peak load force rates (LFR) before liftoff on each trial were used as the dependent variables to examine sensorimotor prediction. If a clear peak was detected (defined as a force rate increase longer than 50 ms to more than 5 N/s and a drop of more than 25% of the peak value before the next increase) before a second higher peak, the value of the first peak was considered to represent prediction. A single trial from one participant in the control group's LFR data was removed due to an early liftoff and thus uncertainty regarding the baseline normalization. These were examined with a mixed design 2 × 2x9 ANOVA with one between-group factor (group: AR, Control) and two within-subject factors (object size: large, small and trial pair: T1-9). The data from the three retention trial pairs were examined in a separate within-subject 2 × 3 ANOVA with factors of object size (large, small) and trial pair (T10, T11, T12).

All data were examined with Mauchly's test of sphericity prior to statistical analysis. Significant main effects and interactions were followed up with paired tests comparing the large-small ratings/forces at each timepoint within each group. All analyses were conducted in Jamovi version 1.21.

3 Results

3.1 Size–weight illusion

Before lifting the objects (T0), we observed overall higher ratings for the large object than the small object (i.e. a significant main effect of Object Size; $F(1,30) = 114.9$, $p < 0.001$, $\eta^2_p = 0.79$), but no main effect of Group ($F(1,30) = 1.1$, $p = 0.31$, $\eta^2_p = 0.03$) or interaction between these variables ($F(1,30) = 0.13$, $p = 0.72$, $\eta^2_p < 0.01$). Participants in both groups thus experienced normal pre-liftoff ratings of heaviness (Fig. 2).

In the timepoints examined during the experimental trials (T1-4), all main effects and interactions involving the

Timepoint variable failed to meet the assumption of Sphericity, so tests involving these factors had their degrees of freedom adjusted with the Greenhouse–Geisser correction. We observed a significant main effect of Object Size ($F(1,30) = 37.9$, $p < 0.001$, $\eta_p^2 = 0.59$), but no significant effect of Timepoint ($F(2,63.0) = 0.97$, $p = 0.056$, $\eta_p^2 = 0.09$) or of Group ($F(1,30) = 1.1$, $p = 0.31$, $\eta_p^2 = 0.03$). There was a significant interaction between Timepoint and Group ($F(2,63.0) = 5.6$, $p = 0.005$, $\eta_p^2 = 0.16$) and between Object Size and Group ($F(1,30) = 7.6$, $p = 0.01$, $\eta_p^2 = 0.20$). The three-way interaction was not significant ($F(1,61.3) = 1.29$, $p = 0.08$, $\eta_p^2 = 0.04$). Due to the presence of significant interactions, we compared the ratings given to the large and small objects across each trial within each group separately. In the Control group's experimental trials, paired t tests (with a Bonferroni-adjusted threshold of 0.0125 for statistical significance) comparing the heaviness ratings given to the large object compared to the small object at each timepoint found significant differences at Timepoint 1 ($t(15) = 5.1$, $p < 0.001$, $d = 1.27$), Timepoint 2 ($t(15) = 6.2$, $p < 0.001$, $d = 1.54$), Timepoint 3 ($t(15) = 8.0$, $p < 0.001$, $d = 2.0$) and Timepoint 4 ($t(15) = 4.9$, $p < 0.001$, $d = 1.23$). In the AR group's experimental trials, these tests revealed no differences in these ratings on Timepoint 1 ($t(15) = 0.03$, $p = 0.97$, $d < 0.01$) and Timepoint 2 ($t(15) = 0.8$, $p = 0.42$, $d = 0.2$), but robust differences on Timepoint 3 ($t(15) = 3.1$, $p = 0.008$, $d = 0.76$) and Timepoint 4 ($t(15) = 5.1$, $p < 0.001$, $d = 1.3$). These patterns of data indicate that the Control group experienced a normal, unchanging SWI throughout the experiment. The AR group, by contrast, experienced no SWI in early trials, but a normal-looking SWI emerged across repeated lifts.

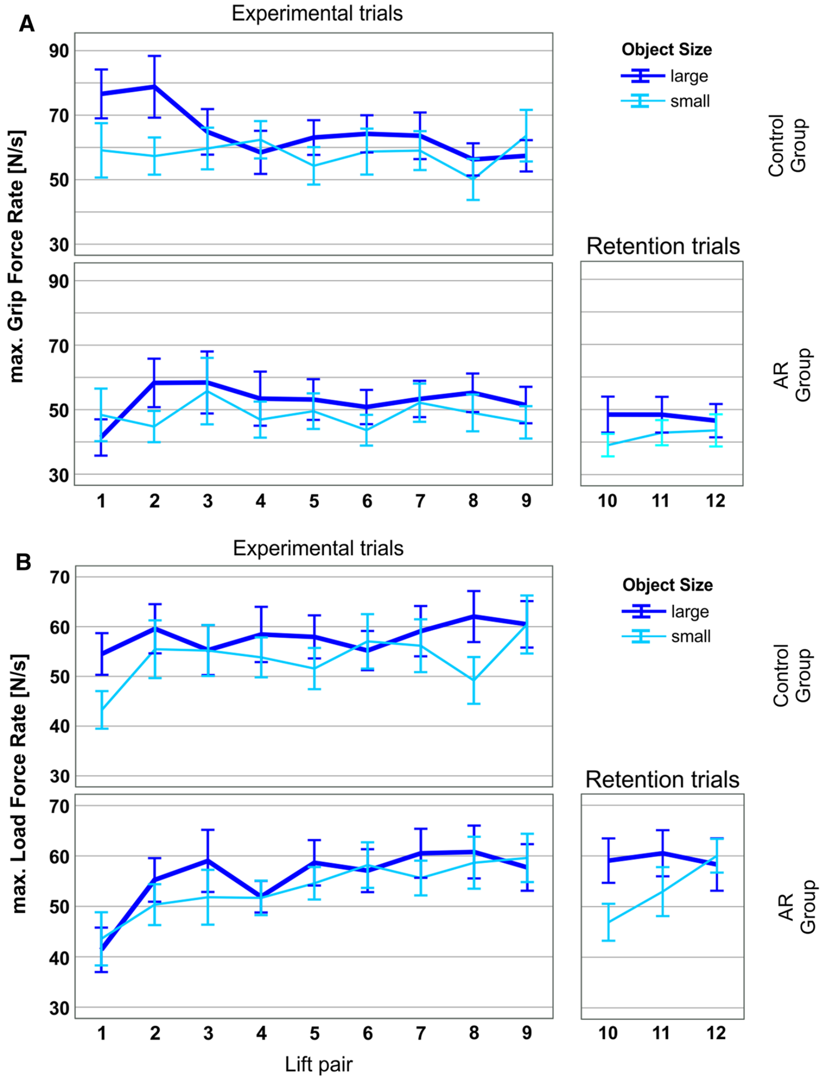
In the timepoints examined during the retention trials (T6, T7), we observed higher ratings for the small object than the large object (i.e. a significant main effect of object size; $F(1,15) = 31.7$, $p < 0.001$, $\eta_p^2 = 0.68$), but no main effect of Timepoint ($F(1,15) = 0.01$, $p = 0.91$, $\eta_p^2 < 0.01$) or interaction between the variables ($F(1,15) = 0.2$, $p = 0.66$, $\eta_p^2 = 0.01$). Paired t tests (with a Bonferroni-adjusted threshold of 0.0125 for statistical significance) comparing the heaviness ratings given to the large object compared to the small object at each timepoint noted significantly higher ratings for the small object at Timepoint 6 ($t(15) = 4.7$, $p < 0.001$, $d = 1.2$) and Timepoint 7 ($t(15) = 5.6$, $p < 0.001$, $d = 1.4$). Participants in the AR group thus experienced a normal SWI after removing the AR glasses.

3.2 Fingertip forces

In the experimental trials (T1-9), in terms of peak GFR (Fig. 3a) all main effects and interactions involving the Trial variable failed to meet the assumption of Sphericity, so tests involving these factors had their degrees of freedom adjusted with the Greenhouse–Geisser correction. We observed a main effect of Object size ($F(1,29) = 15.2$, $p < 0.001$, $\eta_p^2 < 0.001$), but no main effect of Trial ($F(4.03, 116.9) = 1.03$, $p = 0.39$, $\eta_p^2 = 0.03$) or Group ($F(1,29) = 2.08$, $p = 0.16$, $\eta_p^2 = 0.07$). The interaction between Object size and Group ($F(1,29) = 0.42$, $p = 0.52$, $\eta_p^2 = 0.01$) and Object Size and Trial ($F(4.2,121.8) = 1.75$, $p = 0.14$, $\eta_p^2 = 0.06$) were not significant. The interactions between Trial and Group ($F(4.0,116.9) = 2.14$, $p = 0.08$, $\eta_p^2 = 0.07$), as well as the 3-way interaction ($F(4.2,121.8) = 2.15$, $p = 0.08$, $\eta_p^2 = 0.07$), both failed to reach significance due to the corrections for sphericity. As these interactions were borderline, we conducted the within-group analysis reported above for the perceptual ratings of heaviness. In the Control group's lifts, paired t tests (with a Bonferroni-adjusted threshold of 0.0056 for statistical significance) comparing peak GFR of the large object compared to the small object on each trial found that participants used significantly higher rate of force used to grip the large object on Trial 2 ($t(15) = 3.88$, $p = 0.001$, $d = 0.97$). By contrast, in the AR group's lifts, no significant differences emerged (all p values > 0.054). In terms of peak LFR (Fig. 3b) on the experimental trials, all main effects and interactions met the assumption of sphericity. We observed a main effect of Object size ($F(1,28) = 6.17$, $p = 0.019$, $\eta_p^2 = 0.18$) and a main effect of Trial ($F(8,224) = 5.26$, $p < 0.001$, $\eta_p^2 = 0.16$), but no main effect of Group ($F(1,28) = 0.05$, $p = 0.83$, $\eta_p^2 = 0.002$). As no other interactions were significant or borderline (all p values > 0.30), no further post hoc analysis was conducted. In summary, there is some indication that overlaying computer-generated identically sized objects atop physical objects disrupts the normal tendency to grip heavy-looking large objects at a higher rate of force than light-looking small objects.

In the AR group's retention trials (T10-12), all main effects and interactions met the assumption of sphericity. With the GFR data, we observed a significant main effect of Object size ($F(1,15) = 5.06$, $p = 0.04$, $\eta_p^2 = 0.25$), but no main effect of Trial ($F(2,30) = 0.35$, $p = 0.71$, $\eta_p^2 = 0.02$) and no interaction between the variables ($F(2,30) = 1.04$, $p = 0.37$, $\eta_p^2 = 0.07$). For the LFR data, we observed a significant main effect of Object size ($F(1,15) = 5.28$, $p = 0.04$, $\eta_p^2 = 0.26$), but no main effect of Trial ($F(2,30) = 1.19$, $p = 0.32$, $\eta_p^2 = 0.07$). The interaction between the variables was significant ($F(2,30) = 6.03$, $p = 0.006$, $\eta_p^2 = 0.29$), so we compared the force rates used to lift the large and small object on each trial of this phase of the experiment. These paired t tests, with a threshold of 0.017 to achieve statistical significance, revealed that the large object was lifted at a higher rate of force than the small object on Trial 1 ($t(15) = 3.89$, $p = 0.001$, $d = 0.91$), but not the later trials (all p values > 0.04). This analysis suggests that the sensorimotor memories learned

Fig. 3 **a** Peak grip force rate and **b** peak load force rate for the experimental trials (T1-9) across both groups, and for the retention trials (T10-12) for the AR group. Error bars indicate standard error of the mean. The dark blue (black) bars represent the large object and the light blue (grey) bars represent the small object. (Color figure online)



when seeing the computer-generated objects does not transfer to interactions with the physical objects upon which they were overlaid.

3.3 Subjective experience of augmented elements

The experienced presence of augmented objects in the physical environment was assessed using a questionnaire (Regenbrecht and Schubert 2002). The results of the presence questionnaire (Table 2) reveal that our augmented cubes were judged low in realness and seemed to be not integrated well with the real objects (component 1, Mode [Q1&Q2] = 1, Mode [Q3] = 2). Spatial presence of our augmented objects was rated high (component 2). Subjects had the impression that the augmented cubes were located in space and experienced them as three-dimensional (Mode [Q4] = 5, Mode [Q5] = 6). Perceptual stress in our sample size was moderate (component 3). The difference between real and virtual drew the subject´s attention (Mode [Q6] = 2), but the perception of the augmented cubes did not need a lot of effort (Mode [Q7] = 4).

Table 2 Results of the presence questionnaire

	Q1	Q2	Q3	Q4	Q5	Q6	Q7
Median	1	2	2	4	5,5	2	4
Mode	1	1	2	5	6	2	4
Mean (SD)	1.6 (1.3)	2.4 (1.9)	2.6 (1.8)	4.0 (1.3)	4.8 (1.7)	2.3 (1.9)	4.2 (1.5)
Minimum	0	0	0	0	1	0	0
Maximum	4	6	6	5	6	6	6

4 Discussion

This study sought to examine how computer-generated cues to an object's volume, delivered via AR glasses, might affect perceptions of heaviness and the predictive application or fingertip forces in the context of the SWI. Participants lifted and judged the weight of a pair of boxes with the same mass but different volumes. These stimuli typically induce a robust and unchanging perceptual effect whereby the small object feels heavier than the large object, and a transient sensorimotor prediction whereby small objects are lifted at a lower rate of force than larger objects during the initial lifts. Half of the participants lifted these boxes with normal vision, whereas the other half wore AR glasses which overlaid images of identically sized boxes atop the physical stimuli. The Control group, who lifted the boxes without the AR glasses, experienced a strong SWI throughout the experimental trials, and gripped the large box at a higher rate of force than the small box on early trials. Despite being informed about the real physical size differences the AR group, by contrast, experienced no SWI in the early trials, with a robust illusion emerging over repeated lifts. Furthermore, they showed no evidence that the physical size of the cubes affected the way that they gripped and lifted the object. This propensity to favour the AR cues over the cues from the physical environment was further evidenced through retention trials, where participants in the AR group removed their AR glasses and lifted the objects several more times. Here, despite having lifted the boxes enough times to adapt their forces to the true mass, they lifted the large object with a higher rate of force than the small object–as if they had not undertaken the experimental lifts at all.

The findings from this work help better understand the factors which drive the SWI. First, they highlight the important role that visual cues play in the induction of the SWI, with participants (on early trials) appearing to value the cues to volume over the explicitly delivered 'high-level' information about the size of the object on the upcoming lift, which is consistent with recent work showing that the size of a container completely overwhelms cues to how full the container is (Saccone et al. 2019). Similarly, semantic cues are not sufficient to induce an expectation-driven weight illusion (Naylor et al. 2020). The emergence of the SWI in later trials is also interesting and could suggest that the lack of a SWI on early trials was simply a consequence of participants being distracted by the novel visual cues. This hypothesis is not, however, consistent with recent work showing that the SWI is not reduced in the presence of a secondary cognitive task (Freeman et al. 2019). One possibility is that the emergence of the SWI might be related to participants' down-weighting the visual cues which did not elicit strong feelings of realness (Table 2) and instead relying on the objects' centre of mass as a cue to size. The perceptual quality of our augmented cues might further have influenced the size perception. Optical-see-through displays can exhibit under-estimation of size in augmented objects and is affected by the visualization techniques (Ahn et al. 2019). As both of the lifted objects were cubes, participants would have had access to their physical volume through the moment of their inertia tensor, experienced thought slight deviations from a perfectly vertical lift. This cue is well-established as a way to affect perceptions of heaviness (Amazeen and Turvey 1996; Valdez and Amazeen 2008), but the dynamic switch in dominance from vision to haptic size cues over repeated interactions has not, to our knowledge, been reported. Future work undertaking the opposite paradigm, with differently sized objects overlaid atop objects with identical physical volumes, and stimuli which dynamically alter their visual properties during and between trials (van Polanen and Davare 2019), might help disentangle these possibilities. Increasing the sense of realness by integrating a 3D scanned mesh model of the physical cubes might further influence the size perception and potentially the experienced SWI.

Arguably more important, however, are what these findings mean in the context of AR. This technology is being used widely across society, from the resurgence of heads-up displays to overlay key information atop drivers' perspective of the road in cars, to so-called 'smart glasses' such as those employed in the current work. And, while this study is not the first to show that computer graphics can influence perception enough to induce the SWI (Buckingham 2019; Heineken and Schulte 2007; Kawai et al. 2007), it is the first indication that these graphical elements can take precedence over visible cues from the physical environment for a period of time, eliminating an otherwise robust perceptual illusion. The findings related to the fingertip forces during initial lifts is also particularly noteworthy. The control group showed broadly the expected pattern of data, using higher rates of fingertip forces to interact with the large object than the small object on early trials. The AR group, by contrast, lifted both boxes with very similar rates of force from the initial trials, and continued to do so until the end of the study. When the AR goggles were removed, they lifted the boxes as if they were doing so for the first time (i.e. analogous to the control group's initial interactions). Together, these data suggest that the computer-generated objects displayed through the AR goggles were treated by participants' sensorimotor systems as if they were real, in the sense that the artificial cues were prioritized to drive this form of dextrous behaviour. Designers of AR content should take heed that the images overlaid on the physical environment can affect this ostensibly automatic behaviour.

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Author Contributions NR and JH formulated the research question and designed the experiment. AT and NR developed the AR application. LMH recruited and tested the participants. JH, GB, LMH, and NR performed the data extraction and data analysis. GB, NR, and JH drafted the manuscript. All authors contributed to the final draft of the manuscript. All authors read and approved the final manuscript.

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Data Availability All project files are publicly available at the Open Science Framework website: https://osf.io/fz368/ (Rohrbach et al. 2020a). This includes the perceptual data and fingertip force data as well as exemplary videos demonstrating the experimental setup from the first-person perspective.

Code availability The full project code is available on GitHub https://github.com/athierfelder/size-weight-illusion (Rohrbach et al. 2020b).

Declarations

Conflicts of interest The authors declare that they have no competing interests with regards to the submitted work.

Ethics approval Ethical approval for the study was given by the Ethics Committee of the Medical Faculty of the Technical University of Munich (reference number 175/17 S). All participants gave written informed consent.

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3.4 Improvement of apraxia with augmented reality: influencing pantomime of tool use via holographic cues

3.4.1 Visual abstract

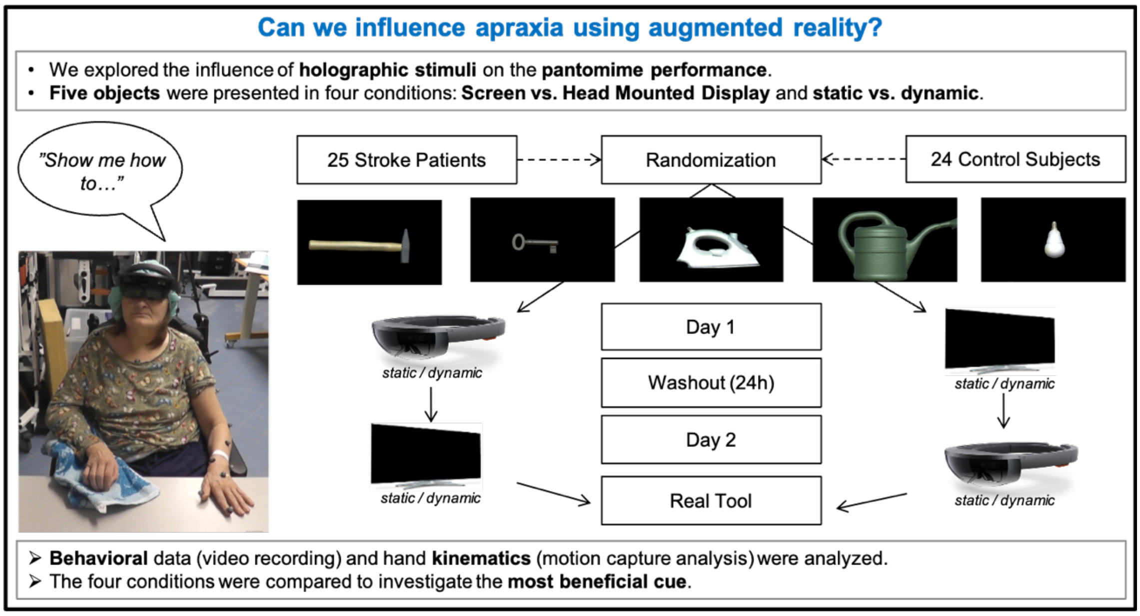

Figure 13. Visual abstract study IV.

Authors: Nina Rohrbach, Carmen Krewer, Lisa Löhnert, Annika Thiefelder, Jennifer Randerath, Klaus Jahn, and Joachim Hermsdörfer

Title: Improvement of apraxia with Augmented Reality: influencing pantomime of tool use via holographic cues

Journal: Frontiers in Neurology

DOI: https://doi.org/10.3389/fneur.2021.711900

Protocol: The protocol was prospectively registered with the German Clinical Trials Register (DRKS) on 22 September 2018 (Trial ID =108 DRKS00015464, Universal Trial Number = U1111-1220-6410).

Data/code: Supplementary data are publicly available at the Open Science Framework website https://osf.io/uakw2/?view_only=a55698fafb6541f7878284bab64e940c. The project code is available on GitHub: https://github.com/Ninarohrbach/panto-holo.

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3.4.2 Summary

Background: Defective pantomime of tool use is a hall mark of limb apraxia. Contextual information has been demonstrated to improve tool use performance. Further, knowledge about the potential impact of technological aids such as augmented reality (AR) for patients with limb apraxia is still scarce. A better understanding of the impact of technological properties (e.g., saliency) and user attributes (e.g., sense of presence) that contribute to motor performances in augmented environments may inform decisions about their use in stroke rehabilitation.

Objective: Since augmented reality technology offers a new way to provide contextual information, we applied it to pantomime of tool use. We hypothesize that the disturbed movement execution can be mitigated by AR stimulation. If visual stimuli facilitate the access to the appropriate motor program in patients with apraxia, the patient's performance should improve with increased saliency, i.e., should be better when supported by dynamic and holographic cues versus static and screen-based cues.

Methods: In this randomized crossover study, 21 stroke patients and 23 healthy control subjects mimed the use of five common objects, presented in two *Environments* (Screen vs. Head Mounted Display, HMD) and two *Modes* (Static vs. Dynamic) resulting in four conditions ($\text{Screen}^{\text{Stat}}$, $\text{Screen}^{\text{Dyn}}$, HMD^{Stat}, HMD^{Dyn}), followed by a real tool demonstration. Pantomime of tool use was analysed by a scoring system using video recordings. Additionally, the sense of presence was assessed using a questionnaire.

Results: Healthy control participants performed close to ceiling and significantly better than patients. Patients achieved significantly higher scores with holographic or dynamic cues. When their pantomime performance was supported by animated holographic cues, it did not differ significantly from real tool demonstration. As the sense of presence increases with animated holograms, so does the pantomime performance.

Conclusion: Patients´ pantomime performance improved with visual stimuli of increasing saliency. Remarkably, pantomiming appeared more equivalent to the real tool demonstration when being supported by animated holograms (e.g., striking hammer). Future assistive technology could be implemented upon this knowledge and thus, positively impact the rehabilitation process and a patient's autonomy.

3.4.3 Author´s contributions

The study was led by TUM and performed in collaboration with the Schön Klinik Bad Aibling, Germany. Nina Rohrbach is the first and corresponding author of this manuscript. All authors contributed to the final draft of the manuscript, read and approved the final manuscript.

Nina Rohrbach:	Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Visualization, Writing – Original draft, Writing – Review & Editing, Funding acquisition
Carmen Krewer:	Writing – Review & Editing, Project administration, Supervision
Lisa Löhnert:	Validation, Investigation, Funding acquisition
Annika Thiefelder:	Software, Visualization
Jennifer Randerath:	Writing – Review & Editing, Resources
Klaus Jahn:	Investigation, Writing – Review & Editing, Resources
Joachim Hermsdörfer:	Conceptualization, Methodology, Formal analysis, Writing – Review & Editing, Supervision, Resources, Funding acquisition

3.4.4 Original publication IV

frontiers in Neurology

ORIGINAL RESEARCH
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Improvement of Apraxia With Augmented Reality: Influencing Pantomime of Tool Use via Holographic Cues

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Methods: Twenty one stroke patients and 23 healthy control subjects were randomized to mime the use of five objects, presented in two *Environments* (Screen vs. Head Mounted Display, HMD) and two *Modes* (Static vs. Dynamic) resulting in four conditions ($Screen^{Stat}$, $Screen^{Dyn}$, HMD^{Stat}, HMD^{Dyn}), followed by a real tool demonstration. Pantomiming was analyzed by a scoring system using video recordings. Additionally, the sense of presence was assessed using a questionnaire.

Results: Healthy control participants performed close to ceiling and significantly better than patients. Patients achieved significantly higher scores with holographic or dynamic cues. Remarkably, when their performance was supported by animated holographic cues (e.g., striking hammer), it did not differ significantly from real tool demonstration. As the sense of presence increases with animated holograms, so does the pantomiming.

Conclusion: Patients' performance improved with visual stimuli of increasing saliency. Future assistive technology could be implemented upon this knowledge and thus, positively impact the rehabilitation process and a patient's autonomy.

Keywords: virtual reality, apraxia, pantomime of tool use, stroke, hologram, sense of presence, visual cues

INTRODUCTION

Apraxia occurs in 30–50% of patients after left brain damage (LBD) (1, 2) and frequently co-occurs with other syndromes, such as aphasia or neglect (3–6). Limb apraxia refers to a higher-order motor disorder of learned purposive movement skills not caused by deficits of elemental motor or sensory systems (7) that may also affect activities of daily living (ADL) (8, 9). Patients show impairments in planning or producing motor actions. Typically, they have problems with gesture imitation, pantomimed tool use, and actual tool use (4, 10, 11). In the pantomime of tool use task patients are asked to produce an action without holding the object in their hand (12). Pantomiming requires both, motor-cognitive (e.g., the spatial configuration of the body, hands and movements) and communicative processes, including the simulative demonstration and integration of semantic and motor features of the underlying tool use action, requiring a heightened demand on the working memory processes (5, 10, 13, 14). Pantomime of tool use is considered as very sensitive in detecting the presence of limb apraxia; typically the pantomime mode appears more sensitive as compared to actual tool use mode (3, 15), however performance measures across these modes correlate and individual patterns appear stable (16, 17). While both modes may retrieve similar concepts, differences may be represented by missing visuotactile feedback, i.e., the absence of mechanical interaction and cues from real objects, the heightened demand on imagery and the translation from mental images to motor execution (5, 10, 11, 16, 18, 19). Contextual information may provide critical cues facilitating the access to an adequate motor concept and may constrain the possibilities for action production (15–17). While tactile feedback alone, such as a stick that resembles the handle of a tool, seems to be inefficient in evoking the correct motor program of an action (20, 21), several studies underlined the role of visual feedback (11, 17, 22). In this regard, it has been shown that the perception of object affordances (i.e., action possibilities offered by the environment and the object's properties) and its visual attributes is influenced by its visuo-perceptual context, such as thematic and functional properties but also by space (23).

Augmented reality (AR) technology provides a unique way to study the contributions of visual information during pantomiming and may help understand the underlying mechanisms of apraxia. This new technology allows manipulating the experimental setting by providing different contextual information. In contrast to virtual reality, in which the user is often immersed in a completely synthetic environment, in AR the user's real environment is not replaced but rather enriched by spatially aligned virtual objects (24). In mixed reality training scenarios, a higher sense of presence, defined as the psychological product of technological immersion (25), is suggested to enhance motor performance (26–28). AR systems are advantageous over virtual reality in providing a better sense of presence and reality judgments because users can still see their body parts when interacting with virtual objects (29). These virtual objects or holograms, herein referred to as the perception of a computer generated object through stereo imaging, can provide detailed visual contextual information about the properties of the object (e.g., size or structure) and its functioning (e.g., a moving hologram showing its intention) by creating a realistic illusion in three dimensions (30). Practicing in a salient environment by using meaningful and context-specific cues is related to induced plasticity, increased motor learning and a transfer to other tasks (31). Saliency is a strong predictor of attention and gaze allocation and as such a crucial factor in most everyday visual tasks and everyday functioning (32–34). While visual salience refers to objective attributes compared to its surroundings (e.g., object color and structure), semantic salience defines associations with an object (e.g., memories or personal importance) and depends on the user (35). We suggest holograms to function as cues with high visual and semantic salience, which might support motor actions in patients with apraxia. This is in line with the most recent concept of "action reappraisal" by Federico and Brandimonte (23), a reasoning-based approach in human tool-use processing, suggesting that tool use actions utilize multiple sources of information, including affordances and contextual conditions.

The main objective of this study was to test the hypothesis that the disturbed movement execution in stroke patients with apraxia can be mitigated by AR stimulation during pantomime tasks. If visual stimuli facilitate the access to the appropriate motor program in patients with apraxia, the performance should improve with cues of higher saliency and more contextual information. Specifically, we consider dynamic holographic tools presented through a Head Mounted Display (HMD) as stimuli with higher salience because the moving character on the one side and the holographic nature (i.e., three-dimensionality) on the other side should attract more attention than two-dimensional static images of a tool, enhancing the perception of the object in this way (33, 36). The enriched contextual environment (e.g., detailed object features such as structure) and the overall realism that is conveyed by these properties should provide more cognitive cues (37). Further, little is known yet as to the impact of the induced sense of presence in virtual environments on motor performance in stroke rehabilitation (26). We suggested the enriched conditions to evoke higher presence, and expected to observe an association between increased presence and pantomime performance. A better understanding of the technological properties (e.g., visual saliency) and user attributes (e.g., presence) that contribute to motor performances in augmented environments may further inform decisions about their use in overall stroke rehabilitation.

METHODS

Participants

This study was conducted at the neurorehabilitation hospital Schoen Clinic Bad Aibling (Germany). From April 2019 to December 2019, we included a total of 49 participants (25 patients

Abbreviations: ADL, Activities of Daily Living; AR, Augmented Reality; DILA-S, Diagnostic Instrument for Limb Apraxia – Short Version; Dyn, Dynamic; EDI, Edinburgh Handedness Inventory; LBD, Left Brain Damage; MI, Motricity Index; MMSE, Mini Mental State Examination; NNPT, Nine Hole Peg Test; Stat, Static.

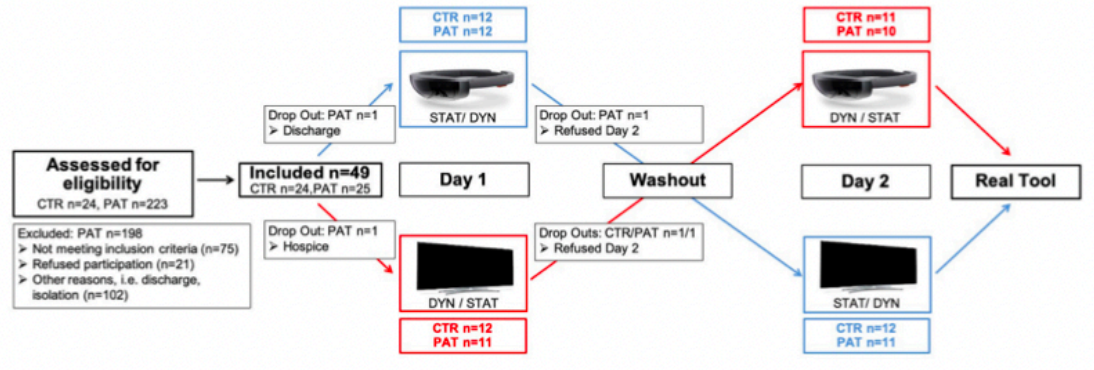

FIGURE 1 | Patients' flow through the study. All participants had to perform the pantomime task twice (Static/Dynamic) in each Environment (HMD/Screen), followed by the real tool condition. The washout time was set to >24 h and did not include any additional tasks. Three participants only completed Day 1 and were excluded from further analyses.

with LBD and 24 healthy age-matched control persons) who fulfilled the eligibility criteria: (1) stroke in the left hemisphere with signs of apraxia (or no stroke in controls), (2) normal or corrected-to-normal vision, (3) sufficient cognitive ability to understand and follow task instructions (tested prior to the study), (4) no other neurological, psychiatric diseases or poor general condition affecting testing (i.e., the patient had to be able to sit for the duration of the experiment). Healthy control participants were recruited via poster announcements distributed in the clinic and University and self-registration. The sample size was based on an estimate on earlier studies comparing different execution conditions for similar actions, in which significant effects were found in comparable samples ($n = 23$ per group) (15, 17). The study was approved by the Ethics Committee of the Medical Faculty of the Technical University of Munich and all participants or their legal representatives provided written informed consent prior to testing, which was performed in accordance to the declaration of Helsinki. The protocol was prospectively registered with the German Clinical Trials Register (DRKS) on 22 September 2018 (TrialID = DRKS00015464, Universal Trial Number = U1111-1220-6410).

Trial Design

Within this randomized crossover study, we tested the influence of varying types of visual stimuli with different degrees of saliency to determine the most effective way of support. Participants had to mime the use of five common objects (hammer, flat-iron, watering can, key, electric bulb) with variable combinations of visual input. On the 1st day, they were randomized 1:1 via sealed envelopes to begin with one of the testing **Environments** (Screen vs. HMD), of which each testing environment was randomized 1:1 to start with one of the testing **Modes** (Static vs. Dynamic). After a 24 h "washout" period, the same task was performed starting with the other testing environment, ending up with four **different combinations**: $\text{Screen}^{\text{Stat}}$, $\text{Screen}^{\text{Dyn}}$, HMD^{Stat}, HMD^{Dyn} (**Figure 1**). Each object was presented four times in a row whereas the first presentation was designed as a familiarization where no action was required, to ensure that participants were able to see the images and minimize an influence of visuo-spatial deficits. The order of object presentation was balanced for these four combinations, and held constant for both testing days (i.e., one out of five predefined sequences of object presentations was assigned to each participant). In the screen environment, participants were supported by images of the objects presented on a laptop monitor (15.6-inch, 1,920 x 1,080-pixel resolution), whereby the viewing distance was held constant among all participants (i.e., in a reachable zone of 70 cm when leaning forwards). In the HMD environment, participants wore the Microsoft HoloLens device (1st generation) to view holographic images. In the dynamic mode, one could see the individual tool moving (e.g., striking hammer) while in the static mode the tool remained still (see **Supplementary Videos 2, 3**). At the end of day 2 after all four conditions were completed, participants had to demonstrate the use of the real tool (in the absence of the target object) that was placed on the table in a standardized way (i.e., the tools were aligned in accordance with the other testing environments, i.e., oriented to promote an action with the left hand as shown in **Figure 2D**), not accompanied by any additional visual input ("Real Tool" condition).

Participants were seated in front of a table, either facing the screen or wearing the HMD (**Figure 2**). To familiarize with the HMD a practice holographic object, i.e., a red paper boat (see **Supplementary Video 1**), was presented accompanied by a standardized explanation of its main technical feature and current limitation of a limited field of view in HoloLens (1st generation). Practice items were included at the beginning of each day by showing printed objects to the participants (fork—corkscrew—saw), and task comprehension was assumed when participants at least attempted to produce a meaningful movement, based on the DILA-S pantomime task recommendations (13). In all conditions participants were

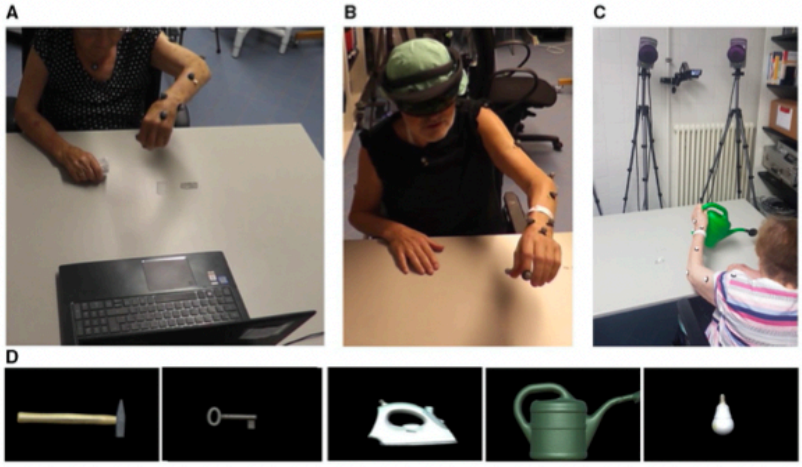

FIGURE 2 | Third person perspective of the experimental setup. **(A)** Screen condition, **(B)** HMD condition, **(C)** Real Tool condition; and **(D)** the first-person perspective of the five objects depicted as screen-based images. Only the tools and not the target items were shown (i.e., the hammer, but not a nail).

verbally instructed by the experimenter (e.g. "please show me how to pound in a nail with a hammer") as described in (13) and were allowed to start miming as soon as the picture of the object became visible. Their movements were videotaped for later observational evaluation. They used their left hand (non-paretic) in all conditions and were tested on consecutive days to reduce carryover effects and fatigue, on about the same time of the day, lasting a maximum of 1 h/day. For patients who still fatigued very fast, the additional clinical testing was postponed to a 3rd day. During testing participants were asked for any discomfort or motion sickness. Neither participants nor examiners were blinded due to the optical see-through device being used.

Software Development

The testing environments were designed using the game engine development tool, Unity 3D (Version 2017.4). The five objects were created by 3D-scanning their real-life counterparts in order to achieve high visual fidelity. Object selection was based on its movement characteristics to cover a variety of different movement components, movement planes and grip formations (e.g., repetitive hammering with elbow flexion/extension using a cylindrical grip in the longitudinal plane). Three of the five gestures involved non-repetitive movements (water a plant, iron a blouse, open a lock), while the other two were repetitive gestures (screw in an electric bulb, hammer a nail). For this study we chose gestures performed without body contact because of the complexity of holographic animations performed on the body. Only the tools and not their corresponding counterpart were shown (i.e., the hammer, but not a nail, see **Figure 2D**). The dynamic version is based on recordings of real tool use movements with the same physical objects (including the recipient object) using motion capturing (Qualisys Inc., Gothenburg, Sweden). The gathered kinematic data were post-processed to handle noise. In the screen environment, the objects had to be adjusted in size in order to be properly displayed on the screen. In the HMD environment, we adjusted the objects' position in space to maintain the objects' real sizes. Further, the objects were oriented in space in a way that the tools' handle functioned as an easy to graspable stimulus (38). The full project code is available at GitHub https://github.com/Ninarohrbach/panto-holo, and a visualization of the object presentations can be found in the supplements (**Supplementary Videos 2, 3**).

Remote Control System

Generally interacting with the HoloLens device as an experimenter is inconvenient, because one would need to put on the device for each single interaction. We solved this problem by using a web application to remotely control the HoloLens application (see **Supplementary Video 1**). The advantage of a web application is that it can be run on almost any device that has a web browser, e.g., smartphones. The complete system consisted of three components: The web application, a webserver and the HoloLens application. The HoloLens application was implemented using Unity 2017.4 using C++. A Firebase application was used as a web server and Polymer 2.0 was used for the front-end of the web application. This way, the experimenter could easily change the values (i.e., object 1–5, and mode "static"/"dynamic") on the Firebase server in real-time. The same system was used for the screen environment, by running the Unity application on a laptop.

Clinical Tests and Questionnaires

Prior testing, participants were asked questions regarding their sociodemographic background and previous HMD experience. The Mini Mental State Examination (MMSE) (39) was conducted to assess cognitive impairment. The Titmus Test (Stereo Optical Co., Chicago, IL) with its two sub-tests was administered to classify for the presence (i.e., House Fly test) and the quality of stereovision (i.e., Circles test). The Edinburgh Handedness Inventory (EDI) (40) was used to assess the dominance of a person's hand in everyday activities before the stroke. To evaluate manual dexterity, we conducted the Nine Hole Peg Test (NHPT) (41). For this purpose, the left (non-paretic) hand was tested twice using motion capture analysis and the mean time of two successful trials was computed (see "hand kinematics" in data analysis). Further, we examined the Motricity Index (MI) to evaluate the extent of the paralysis of the affected arm by assessing the strength (remaining force) of shoulder abduction, elbow flexion and finger griping (42). To diagnose for the presence of apraxia the Diagnostic Instrument for Limb Apraxia—Short Version (DILA-S) was used (13). Note, that the DILA-S was evaluated for patients with LBD and is applicable for patients with severe aphasia or neglect. At the end of each testing condition (i.e., four times), participants completed a slightly adapted presence questionnaire (43) (**Supplementary Table 1**).

DATA ANALYSIS

Scoring System

Supplementary Table 2 provides details on the scoring procedure. As the primary outcome parameter, a performance scoring was undertaken. For task evaluation we adapted the **Production scale** (PS) (13) in which four movement components were rated on a three-point scale resulting in a maximum score of 24 points per object and condition after three trials. Additionally, we applied the **Interaction scale** (IS) developed for the purpose of this study to investigate the participants' interaction with the different cues. With the standard pantomime procedure in clinical settings the examiner sometimes observes patients who seemingly try to interact with the presented item by reaching for and touching the depicted picture. One point per trial was given if participants actively tried to reach forward and grasp the virtual object or followed the movement, ending up with a maximum of three points per object and condition after three trials. Note that our experimental task and digital content do not require any interaction. Thus, the term "interaction" within this study does not reflect the overall accepted definition in the AR domain [for a recent review on immersive systems (44)].

Each participant's videotaped performance was viewed in its full length four times, once for each of the four movement parts. Two independent raters (NR, LL) scored the first 20 participants (10 patients, 10 controls) and critical aspects were discussed within the research team in a consensus meeting. Validating a certain percentage of the study sample by two independent evaluators is common and widely accepted practice e.g., 25% in (18) and (45). The inter-rater reliability of the pantomime scoring (400 data points for the Production and Interaction scale) and real tool scoring (50 data points) of the first ten healthy control subjects achieved large results for pantomiming (Kendall's Tau $\tau = 0.643$ for Production; $\tau = 0.602$ for Interaction) and real tool demo ($\tau = 0.862$). After further refinement of the system, all data were scored and uncertainties were collaboratively discussed until the two raters met consensus.

Statistical Analysis

All outcome variables were tested for normal distribution using Shapiro-Wilk's test. The statistical analysis included a *t*-test for age and non-parametric tests for sex, stereovision, MMSE and NHPT-time to determine if there were differences between the patient and the control group. For the pantomime performance (averaged score across all five objects for each of the four conditions) and the subjective experience of the presented objects (calculated mean score of presence data for each of the four conditions) a mixed repeated measures $2 \times 2 \times 2$ ANOVA was conducted to determine whether any changes in the dependent variables (Production Scale, Interaction Scale) were caused by the between-subject factor *Group* (Stroke, Control), the within-subject factors *Environment* (Screen, HMD) and *Mode* (Static, Dynamic), or their interactions. We dealt with missing values (Production: 2.06%, Interaction: 2.14%) by imputing the mean performance value for the respective object and condition (46). Significant interactions, simple effects and main effects were followed-up with Bonferroni-adjusted pairwise *post-hoc* tests comparing the performance scores of the different visual cues. The achieved real tool scores were compared separately between groups using independent *t*-tests. They were further analyzed within each group, by comparing them with the means of the four combinations of the pantomime task using *t*-tests for paired samples. We calculated the performance effects, i.e., the environmental (HMD-Effect), the conditional (DYN-Effect) and the combined effect (HOLO-Effect) for both scales, defined as the following:

- HMD-Effect = Mean (HMD^{Stat}, HMD^{Dyn}) – Mean ($Screen^{Stat}$, $Screen^{Dyn}$)
- DYN-Effect = Mean (HMD^{Dyn}, $Screen^{Dyn}$) – Mean (HMD^{Stat}, $Screen^{Stat}$)
- HOLO-Effect = Mean HMD^{Dyn} – Mean ($Screen^{Stat}$, $Screen^{Dyn}$, HMD^{Stat})

We assessed the relationship of the Production and Interaction scores within each group using Spearman's rank correlation (r_s). Further, the performance effects were correlated with the clinical data to test whether the timing of stroke onset, mental capacity, manual dexterity, stereovision or apraxia affect pantomime of tool use using Pearson's r or Spearman's correlation. The relationship between presence and pantomiming was analyzed for each condition within the patient group. For significant correlations, the magnitude was classified considering the following categories: $|r| \geq 0.10$ = small, $|r| \geq 0.30$ = medium and $|r| \geq 0.50$ = large (47). Data analysis was carried out in SPSS (version 26), and the level of significance was established at a 0.05 alpha-level (two-sided).

Hand Kinematics

In addition, we recorded hand movements (a spherical marker attached to the subject's left back of the hand) using motion capturing. Movements were recorded by three cameras (Oquus, Qualisys Inc., Gothenborg, Sweden) and a sample rate of 120 Hz.

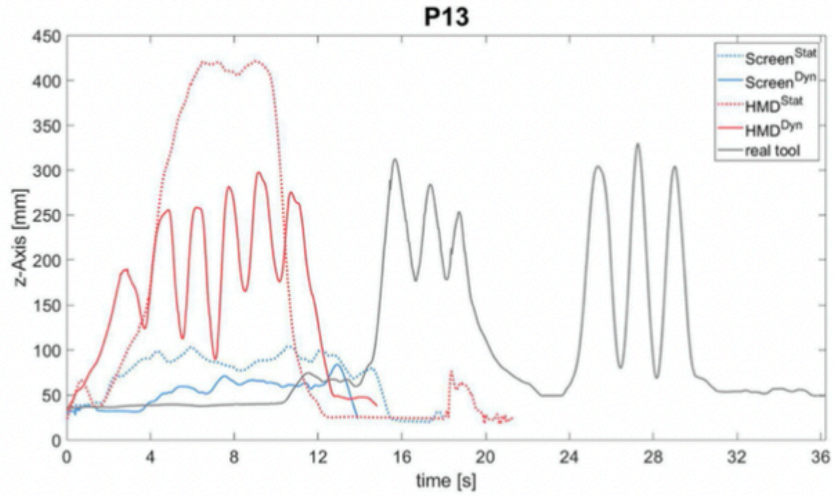

FIGURE 3 | Trajectories of hand movements in patient P13 attempting to pantomime the typical use of a hammer during the different experimental conditions is illustrated: Screen^{Stat} (blue line), Screen^{Dyn} (blue dotted line), HMD^{Stat} (red line), HMD^{Dyn} (red dotted line), real tool (gray line). The complete trajectory along the z-Axis in (mm) during the third of three trials is always shown.

TABLE 1 | Participant's demographics and clinical characteristics.

	LBD ($N = 21$)	Controls ($N = 23$)	Between-Group Comparisons
Sex: male/female	10/11	10/13	$t_{(42)} = -0.988$, $p = 0.329$
Age: mean years (range)	69.81 (41–91)	65.87 (40–91)	$U = 231.5$, $Z = -0.272$, $p = 1.0$
Adverse events, side effects*: yes/no	0/21	0/23	
EDI: right/left/both	20/0/1	23/0/0	
Education level**: low/middle/high	8/8/4	6/7/10	
Experience with HMD: yes/no	0/21	0/23	
Etiology: Ischemic infarct/ICB	18/3	NA	
Aphasia***: yes/no	15/6	NA	
MMSE: mean (range)	21.25 (14–28), $N = 16$	28.83 (24–30)	$U = 8.500$, $Z = 34.6$, $p < 0.001$
MI: mean (range)	52.6 (0–100)	NA	
Neglect****: yes/no	6/15	NA	
NHPT: mean time in seconds (range)	47 (26–140)	24.5 (18.5–44)	$U = 445.00$, $Z = 42.5$, $p < 0.001$
Titmus Test			
House Fly: stereovision given (yes/no)	13/6	23/0	$U = 138.0$, $Z = -3.151$, $p = 0.002$
Circles: ≤/> 100 arc/sec	2/16	17/6	$U = 77.0$, $Z = -3.953$, $p < 0.001$
Time since event: mean duration in days (range)	250,7 (11–1,933)	NA	
Visual aids during testing: yes/no	12/9	21/3	

*EDI, Edinburgh Hand Inventory; HMD, Head Mounted Display; ICB, Intracranial bleeding; LBD, Left Brain Damage; MMSE, Mini Mental State Examination; MI, Motricity Index; NA, Not applicable; NHPT, Nine Hole Peg Test (left hand); t, t test for independent samples; U, Mann-Whitney-U-Test, * based on verbal reports, ** Education level: low = secondary school, middle = intermediate school =, high = high school or higher, ***based on Aachen Aphasia Test (AAT) analysis description, i.e., a combination of the subscales Token Test and written language, **** based on different severity levels assessed with different assessments; information provided by neuropsychologists out of a test battery including several paper-pencil tests.*

The kinematic approach served as an objective and sensitive analysis to evaluate the NHPT data and to provide an additional visual illustration to our qualitative findings. Based on the performance results, the patient with the strongest HOLO-Effect (see statistical analysis for further specification) was chosen for further kinematic analysis. Post-processing of the hammering performance (repetitive up and down movement) of P13 was performed using MATLAB R2018b (MathWorks, Natick, MA, USA). We determined the starting and the ending time points by calculating the overall marker velocity in 3D space and thresholding it at $v_{th} = 0.012$ [m/s]. The vertical axis of the movement was extracted and plotted for visualization (**Figure 3**).

RESULTS

Participant Demographics

Participant characteristics and patient-specific information are provided in **Tables 1**, **2**. All but one patient (P23) showed signs of apraxia in at least one of the DILA-S sub-tests (**Supplementary Table 3**), with most patients being affected in the Imitation of gestures (meaningless: 95%, meaningful: 67%), in the Pantomime task (Production: 76%, Execution: 71%) and in the Naturalistic Action Task (NAT: 62%). While the majority of patients had at least mild problems in the Familiar Tools Task (FTT; Selection: 33%, Production: 67%, Execution: 62%) they were less frequently affected in the Novel Tools Task (NTT; Selection: 52%, Production: 29%, Execution: 29%).

Performance Results

Figure 4 displays the performance scores of both groups of the Production and Interaction scales, and **Table 3** shows the ANOVA results respectively. The individually achieved environmental (HMD-Effect), modal (DYN-Effect) and combined (HOLO-Effect) effects in patients are visualized in **Figure 5**. During HMD trials, the key was not visible for three patients (P1&P6: Key_HMD^{Stat}, P1&P16: Key_HMD^{Dyn}), and in another patient (P21) the Screen^{Stat} condition was not videotaped. Overall, we had a total of 26 missing data points out of 1,260 observations on the Production scale (2.06%) and 9 out of 420 on the Interaction scale (2.14%), respectively.

Production Scores

On the Production scale, a significant main effect of *Group* with overall higher scores in controls (**Figure 4A**) indicates that healthy subjects performed significantly better than patients (MD = 6.5; 95%-CI [4.1,8.9], $p < 0.001$). Further, we found significant main effects of *Environment, Mode* and significant interactions between *Environment* × *Group, Mode* × *Group*, and *Environment* × *Mode* × *Group*, but not between *Environment* × *Mode* (**Table 3**).

Next, we analyzed the different combinations within each group separately. Control participants reached almost maximum scores independent of the presented stimuli (M = 23.2, SD = 0.64 [21.4,23.9] with no significant effects or interactions ($p > 0.144$). In patients, we found a statistically significant effect of *Environment* and of *Mode*, but not between *Environment* × *Mode*. Bonferroni-adjusted pairwise comparisons indicate a better performance with the help of holographic (−1.2; 95%-CI [−2.1,−0.19], $p = 0.021$) or dynamic cues (−0.91; 95%-CI [−1.7,−0.16], $p = 0.019$).

Interaction Scores

We found a significant main effect of *Group* on the Interaction scale, suggesting that healthy subjects interacted significantly more with the presented stimuli (0.48; 95%-CI [0.10,0.86], $p = 0.014$; **Figure 4C**). Similar to the Production scores, we found significant main effects of *Environment* and of *Mode*, and a significant *Environment* × *Group* interaction which was driven by higher means in the HMD Environment in controls (Screen: 0.30; 95%-CI [0.13,0.47], HMD: 1.9; 95%-CI [1.4,2.4] compared to patients (Screen: 0.21; 95%-CI [0.11,0.32]; HMD: 1.0; 95%-CI [0.56,1.4]. All remaining interactions were non-significant ($p > 0.518$, **Table 3**).

In both groups, there was a significant effect of *Environment*, suggesting stronger effects of holographic than screen-based cues (Patients: −0.79; 95%-CI [−1.2,−0.39], $p < 0.001$; Controls: −1.6; 95%-CI [−2.1,−1.1], $p < 0.001$). A significant effect of *Mode* in patients and a borderline significant effect of *Mode* in controls ($p = 0.054$) point toward a higher effect of dynamic than static cues (Patients: −0.24; 95%-CI [−0.38,−0.11], $p = 0.001$; Controls: −0.27; 95%-CI [−0.54,0.005], $p = 0.054$).

Correlations Between Production and Interaction Scores

We found medium to large significant correlations between the Production and Interaction scores. In patients, higher interactions with animated screen-based objects were significantly associated with a better performance (Screen^{Dyn} $r_s = 0.699$, $p < 0.001$). In controls by contrast, when the interaction with static holographic items increased, the performance decreased (HMD^{Stat} $r_s = -0.537$, $p = 0.008$). All other correlations were non-significant (**Supplementary Table 4**).

Real Tool Comparison

Patients had significant problems demonstrating the real tool use ($M = 18.3$, $SD = 3.9$) compared to controls [$M = 23$, $SD = 0.74$, $t_{(42)} = 5.7$, $p < 0.001$]. In healthy subjects, all pairwise comparisons were non-significant ($p > 0.208$). In patients, there was a significant difference between real tool use ($M = 18.3$, $SD = 3.9$) and the Production scores achieved in Screen^{Stat} [$M = 15.9$, $SD = 5.8$, $t_{(20)} = 3.7$, $p = 0.001$], Screen^{Dyn} [$M = 16.3$, $SD = 6.0$, $t_{(20)} = 3.0$, $p = 0.007$], and HMD^{Stat} environments [$M = 16.5$, $SD = 6.6$, $t_{(20)} = 2.4$, $p = 0.027$]. In contrast, there was no difference between real tool use and the Production scores observed in the HMD^{Dyn} environment [$M = 17.9$, $SD = 5.6$, $t_{(20)} = 0.75$, $p = 0.461$), suggesting that the performance was best when either receiving dynamic holographic cues or when demonstrating real tool use (**Figure 4**).

Correlations Between Clinical Data and Pantomime Performance Effects

On the Production scale, a higher DYN-Effect was associated with a higher Circles score ($r_s = 0.524$, $p = 0.026$), a higher NHPT time ($r_s = -0.695$, $p < 0.001$), and a lower NTT Selection score ($r_s = -0.498$, $p = 0.021$). On the Interaction scale, a lower DYN-Effect goes along with a lower MMSE score ($r = 0.550$, $p = 0.027$), and with worse performances in object-interaction tasks (FTT Production $r_s = 0.510$, $p = 0.018$; NAT $r_s = 0.546$, $p = 0.013$).

TABLE 2 | Patient's characteristics.

ID	Sex	EDI	Age (y)	ICD-10	Etiology	Stage*	Neglect	Aphasia	MI	NHPT (t)	Stereovision	MMSE
P01	M	right	64	I61.2	ICB	sub-acute	no	Yes	76	42,44	intact	NA
P02	M	right	51	I61.0	ICB	sub-acute	yes	Yes	11	27,77	NA	19
P03	F	right	85	I63.4	Infarct	sub-acute	no	Yes	77	30,51	NA	25
P04	F	right	71	I63.5	Infarct	sub-acute	no	Yes	0	26,18	intact	21
P05	M	right	41	I63.3	Infarct	chronic	no	Yes	0	28,89	impaired	NA
P06	F	right	89	I63.4	Infarct	sub-acute	no	Yes	0	58,38	impaired	NA
P07	M	right	64	I63.4	Infarct	sub-acute	no	Yes	66	30,18	intact	23
P08	M	right	69	I63.2	Infarct	sub-acute	no	Yes	100	81,78	intact	24
P09	M	right	80	G82.29	Infarct	sub-acute	no	No	76	39,50	intact	24
P10	F	right	90	I63.4	Infarct	sub-acute	no	No	88	42,12	impaired	17
P11	M	both	74	I63.4	Infarct	sub-acute	no	Yes	77	39,04	intact	19
P13	F	right	61	I63.4	Infarct	chronic	yes	Yes	78	139,66	impaired	NA
P14	F	right	54	I63.0	Infarct	sub-acute	yes	No	39	59,01	impaired	26
P16	F	right	85	I.63.4	Infarct	chronic	no	Yes	0	61,05	intact	NA
P17	M	right	83	I.63.1	Infarct	sub-acute	no	Yes	100	42,78	intact	14
P18	F	right	72	I63.0	infarct	sub-acute	no	No	0	25,94	intact	19
P19	M	right	65	I63.4	Infarct	sub-acute	yes	Yes	100	68,68	impaired	16
P20	M	right	56	I61.1	ICB	sub-acute	no	Yes	83	28,79	intact	28
P21	F	right	91	I63.5	Infarct	chronic	no	No	100	37,87	intact	21
P22	F	right	79	I67.88	Infarct	sub-acute	yes	Yes	34	52,03	intact	25
P23	F	right	42	I63.5	Infarct	chronic	yes	No	0	26,62	intact	19

Due to communication problems, not all patients could be tested for stereovision and cognition, but comprehension was sufficient to follow task instructions and all patients were able to complete the AR-testing.
*EDI, Edinburgh Hand Inventory; F, Female; ICB, Intracranial bleeding; ICD-10, International Classification of Diseases-Tenth Revision; M, Male; MMSE, Mini Mental State Examination; MI, Motricity Index; NA, Not applicable; NHPT(t), Nine Hole Peg Test (time in seconds, with left hand). *Stage: Sub-acute= <6 months, chronic: >6 months.*

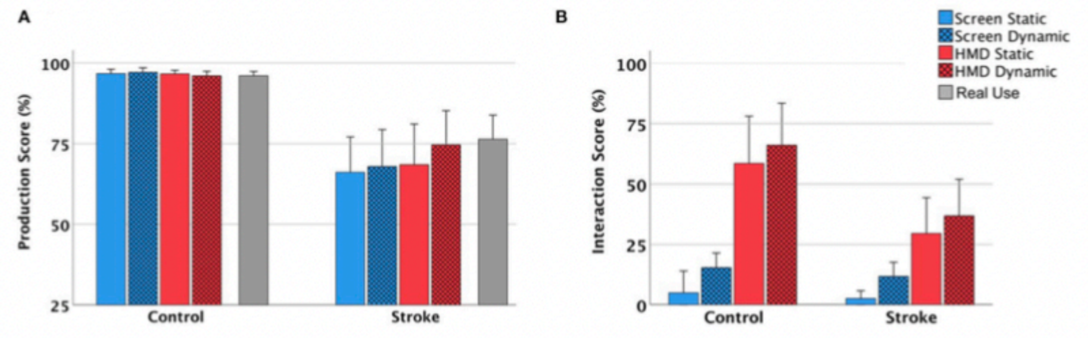

FIGURE 4 | (A,B) Results of the pantomime performance of the control group (left) and stroke group (right); Mean and 95% confidence interval values for the interactions of Environment (HMD/Screen) and Mode (static/dynamic) in **(A)** Production scale and **(B)** Interaction scale are reported.

Further, a non-significant trend between stereovision and the HOLO-Effect^{IS} points toward more frequent interactions with animated holographic items when a higher quality in stereovision is given ($r_s = 0.449$, $p = 0.061$). All other correlations between any of the calculated effects and the clinical tests failed to reveal statistical significance. See **Supplementary Tables 5, 6** for correlations with clinical data and DILA-S results.

Kinematic Analysis

Kinematic analyses were run in order to visualize the qualitative findings. **Figure 3** exemplarily depicts the kinematic analysis for patient 13 who experienced the strongest "HOLO-Effect" based on the results of the performance scoring (**Figure 5**). The complete trajectory along the z-Axis in (mm) of the most successful version of each condition is always shown

TABLE 3 | ANOVA summary for production scale, interaction scale and sense of presence.

Production Scale	**Statistical parameters**					
	***F*(df)**		***p***		**Effect size η_p^2**	
Group	$F_{(1,42)} = 28.6$		<0.001		0.405	
Environment	$F_{(1,42)} = 4.9$		0.031		0.106	
Mode	$F_{(1,42)} = 6.2$		0.017		0.129	
Group × Environment	$F_{(1,42)} = 8.2$		0.007		0.163	
Group × Mode	$F_{(1,42)} = 6.8$		0.012		0.140	
Environment × Mode	$F_{(1,42)} = 1.7$		0.203		0.038	
Group × Environment × Mode	$F_{(1,42)} = 4.5$		0.039		0.097	
	Healthy subjects			**Patients**		
	***F*(df)**	***p***	**Effect size η_p^2**	***F*(df)**	***p***	**Effect size η_p^2**
Environment	$F_{(1,22)} = 1.9$	0.176	0.082	$F_{(1,20)} = 6.2$	0.021	0.238
Mode	$F_{(1,22)} = 0.05$	0.826	0.002	$F_{(1,20)} = 6.5$	0.019	0.244
Environment × Mode	$F_{(1,22)} = 2.3$	0.144	0.095	$F_{(1,20)} = 2.9$	0.103	0.127
Interaction Scale						
	***F*(df)**		***p***		**Effect size η_p^2**	
Group	$F_{(1,42)} = 6.5$		0.014		0.135	
Environment	$F_{(1,42)} = 55.8$		<0.001		0.570	
Mode	$F_{(1,42)} = 11.3$		0.002		0.213	
Group × Environment	$F_{(1,42)} = 6.1$		0.017		0.127	
Group × Mode	$F_{(1,42)} = 0.03$		0.862		0.518	
Environment × Mode	$F_{(1,42)} = 0.43$		0.518		0.010	
Group × Environment × Mode	$F_{(1,42)} = 0.01$		0.932		0.000	
	Healthy subjects			**Patients**		
	***F*(df)**	***p***	**Effect size η_p^2**	***F*(df)**	***p***	**Effect size η_p^2**
Environment	$F_{(1,22)} = 39.9$	<0.001	0.645	$F_{(1,20)} = 17.7$	<0.001	0.470
Mode	$F_{(1,22)} = 4.16$	0.052	0.159	$F_{(1,20)} = 13.5$	0.001	0.403
Environment × Mode	$F_{(1,22)} = 0.20$	0.657	0.009	$F_{(1,20)} = 0.277$	0.605	0.014
SENSE OF PRESENCE*						
	***F*(df)**		***p***		**Effect size η_p^2**	
Group	$F_{(1,34)} = 0.120$		0.731		0.004	
Environment	$F_{(1,34)} = 27.9$		<0.001		0.450	
Mode	$F_{(1,34)} = 0.28$		0.601		0.008	
Group × Environment	$F_{(1,34)} = 5.5$		0.025		0.139	
Group × Mode	$F_{(1,34)} = 0.48$		0.494		0.014	
Environment × Mode	$F_{(1,34)} = 0.02$		0.886		0.001	
Group × Environment × Mode	$F_{(1,34)} = 0.27$		0.605		0.008	

**A few participants did not answer Q3 (HMD^{Stat}: C8, C9, P20; HMD^{Dyn}: C9, P20), herein, we imputed the mean within each group. Eight patients did not or only partially fill in the presence questionnaire (P4, P6, P10, P12, P13, P14, P15, P16), thus, we included 36 data sets in the mrANOVA (Controls n = 23, Patients n = 13).*

(here, the third of the three trials, respectively). In real tool demonstration she failed during the first (Production: 0 points) and second attempt (Production: two points for grip formation when grasping the hammer), but she managed to perform a nice hammering movement (Production: seven points, −1 because of a distorted movement orientation) after some hesitation in her last trial ("conduite d'approche," after all it still took her 10 s to initiate the action). All her attempts to pantomime hammering

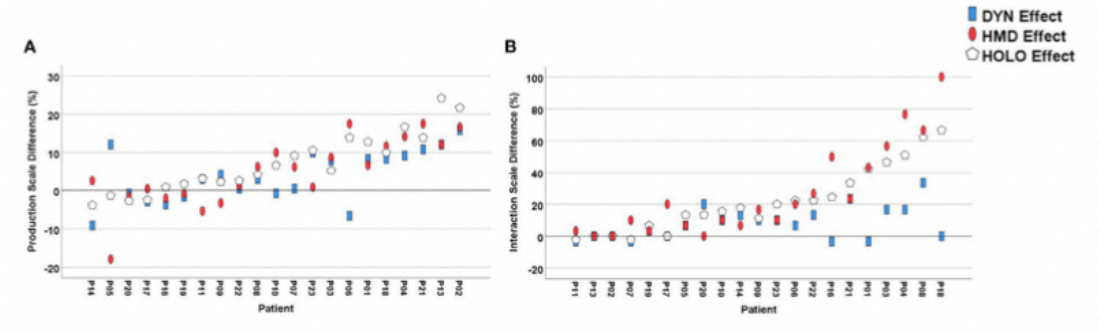

FIGURE 5 | Conditional (DYN), environmental (HMD) and combined (HOLO) effects of individual patients displayed in **(A)** Production Scale and **(B)** Interaction Scale.

in Screen^{Stat}, Screen^{Dyn}, and HMD^{Stat} were characterized by "toying" (Production: zero points in all conditions, respectively). In the HMD^{Dyn} condition by contrast, she presented clear up- and downwards hits with the support of the animated holographic hammer during her second and third attempts (Production: seven points in both attempts; −1 because of distorted grip formation). Note, P13 was randomized to receive HMD-based cues first, followed by screen-based cues on day 2. The corresponding video can be found in the supplements (**Supplementary Video 4**). The analyses demonstrated that the qualitative findings can be verified by kinematic trajectories showing a clear improvement with HMD^{Dyn} support (HOLO-Effect).

Sense of Presence

The statistics is shown in **Table 3**. The two groups did not differ significantly ($p = 0.731$). We found a significant main effect of *Environment* and a significant *Environment* × *Group* interaction, which was driven by a higher sense of presence in the HMD than in the screen environment (Controls^{Screen}: 2.9, 95%-CI [2.4,3.4], Controls^{HMD}: 4.7, 95%-CI [4.4,4.9], Patients^{Screen}: 3.3, 95%-CI [2.7,4.1], Patients^{HMD}: 4.1, 95%-CI [3.7,4.3]). Realness of the presented objects was rated as high in the screen environment ($M = 3.4$, $SD = 1.8$) and very high in the HMD environment ($M = 4.8$, $SD = 1$). While spatial presence was judged low in the screen environment ($M = 2.4$, $SD = 1.9$) it was rated as very high in the HMD environment ($M = 5.1$, $SD = 1$). Perceptual stress was perceived as moderate in both environments (Screen $M = 3.4$, $SD = 1.2$; HMD $M = 3.4$, $SD = 1.4$). All other effects and interactions were non-significant ($p > 0.494$).

Correlations Between Presence and Pantomiming

We found a significant correlation between presence and HMD^{Dyn} Production results ($r = 0.534$, $p = 0.049$), suggesting that as the sense of presence increases with animated holograms, so does the performance. All other correlations were non-significant (**Supplementary Table 7**).

DISCUSSION

In this study the effects of pantomiming with visual feedback provided in different environments (Screen vs. HMD) and different modes (static vs. dynamic) and the impact of presence in each condition were compared. Age-matched control participants performed as expected, close to ceiling in all conditions and significantly better than patients. In contrast, the patients' performances were dependent upon the type of visual feedback given. As hypothesized, patients achieved significantly higher scores when they received holographic (HMD-Effect) or dynamic cues (DYN-Effect). Despite not reaching the level of significance, best results were observed with dynamic holograms (HOLO-Effect, **Figure 5A**). Impressively, single patients improved their overall performance of up to 24% with this form of visual support. The kinematic analysis of one particularly impressive patient (P13), who failed in all conditions except when cued with animated holograms, is shown in **Figure 3** and **Supplementary Video 4**.

A key finding within this study is that pantomiming tended toward the real tool demonstration performance with the support of visual stimuli of increasing salience (**Figure 4A**). It has been hypothesized that different representations underline pantomimed actions and real tool use, with pantomimes serving communication (when trying to enable others to recognize the pretended actions) while real tool actions being instrumental (10, 17, 21, 48). One possible explanation for behavioral improvement when presented with salient stimuli is that the provided holographic cues facilitated compensatory action simulation processes by triggering activities in relevant cortical areas for pantomime of tool use (49). Lesion symptom mapping studies show that defective pantomime of tool use is associated with damage in left ventro-dorsal regions (14, 50, 51), with communicative aspects being related to rather anterior regions in the inferior frontal cortex, and aspects related to motor cognitive movement production being rather associated with posterior regions in the network (5). The latter lesion correlates in left parietal regions are in line with those reported to go along with deficient demonstration of tool use (52). Given the salient nature of holographic presentations of familiar objects one may hypothesize that more specific neural responses in ventral visual streams have been elicited by object recognition processes. Present information about the object may help to specify potential actions by narrowing down action opportunities supported by rather posterior and dorsal regions. Perhaps these processes elicited by the salient cues may help channeling higher-order functions such as attention and reduce the load on action simulation processes in a left fronto-temporo-parietal network. In line with this idea, the visual streams in the ventral and dorsal cortex, that are responsible for perceiving and interacting with common objects in the three-dimensional space, have been shown to respond similarly in AR tasks as compared to real-world tasks (53). Thus, one reason for improved pantomiming might be that the increased saliency in visual input has shifted the pantomime actions from communicative gestures to rather instrumental actions.

Clearly, a strength of this study lies in the design of holograms by 3D-scanning the original tools and recording its real use. The induced sense of presence was significantly higher in HMD than in screen environments, and in the HMD^{Dyn} environment pantomiming improved significantly with higher presence ratings. The realness and high spatial presence evoked by our holograms may have made pantomiming less symbolic as it was rather influenced by the strong external cues. Further, it has been shown that apraxics have deficits in intrinsic coordinate control (11, 22). In such, participants might have extrinsically coordinated their movements in reference to the dynamic or holographic objects. The context factors in the HMD environment, e.g., the orientation in space (designed in a way to invite the participant to reach for it) and the real-sized holograms might have reduced the opportunities of grip formation and movement orientation, thereby limiting the degrees of freedom. Moreover, the structural and texture information, including light reflections, given in our holograms could have helped patients (37). These details became even more extensive in HMD^{Dyn} conditions, offering different perspectives, such as the view of the bottom of the watering can when it is moved. For instance, some patients showed clear difficulties in spatial orientation in screen conditions, but the holographic presentations helped them orientating in space correctly.

Lastly, the dynamic presentation in both environments might have attracted more attention and have had a more prompting character stimulating the correct movement content (20). In this regard, we observed individual patients trying to copy the shown movements, e.g., by following the rhythmic beat of hammering. In neuroimaging studies investigating healthy people, a larger response in the lateral temporal cortex relative to the ventral cortex has been shown when dynamic compared to static humans and tools are viewed, suggesting the lateral temporal cortex to be responsible for complex motion processing (54). Potentially, the moving cues enhanced the activity in the lateral temporal cortex which may have been integrated into the perception-action network processing pantomimes.

This can be partially supported by the Interaction scores, showing significant higher object interactions in HMD or DYN conditions. In patients, higher interactions during the $Screen^{Dyn}$ condition even significantly correlated with increased Production scores, which indicates an added value of dynamic cues in screen-based systems. In addition, patients with a higher quality in stereovision, a better manual dexterity and worse mechanical problem solving benefit more from dynamic cues. One possible explanation is that patients with mechanical problem solving deficits may profit from the increasing visual and semantic information consistent with the task provided by the three-dimensional cues from the HoloLens (e.g., when focusing perception on the best suited affordances to solve the task, here the correct representation of the moving tool). Indirectly, this could be taken as an indicator of an important role of mechanical problem solving in tool use behavior and would therefore be in line with the reasoning-based approach to human tool use (23, 55, 56).

Nevertheless, correlations between Interaction and Production scores during HMD conditions did not become significant ($p > 0.22$). In contrast, and probably even more striking, the patients who experienced the strongest HOLO-Effects on the Production scores (P13, P02) did not interact with the given cues at all (**Figure 5**). Moreover, in healthy subjects the interactions with static holograms even negatively influenced performance, in a way that they changed their motor behavior resulting in unnatural, error-loaded movements when trying to reach for holograms. Potentially, these participants got distracted from the actual task by volitionally directing their attentional focus on the salient cues (36), resulting in more errors. That is, consistent with the results of a feasibility study on AR-based ADL support, the unnatural interaction with holographic animations that impaired the performance by requesting its own resources (57). We would have expected higher presence to result in more interactions with the virtual objects. However, we did not find a significant correlation which can be explained by the experimental task design not *requiring* any real interaction. Still, at this point it remains unclear why some participants were very responsive to the stimuli (such as P18, who interacted with holograms in 100% of the HMD conditions), while others seemed not to respond at all (**Figure 5**). The interaction with dynamic objects was higher in controls as well as in patients with a higher mental state, a better FTT Selection and NAT score. Possibly, unimpaired people are more prone to interacting with holograms because they have more cognitive resources to focus on the augmented information, but this hypothesis has to be further investigated.

Another likely explanation for the improvements is that both the dynamic and holographic information provided error signals for the perceptual-motor system as suggested by Jax et al. (11). While patients with apraxia often struggle in movement preparation (i.e., planning) the adjustment of the movement plan (i.e., online correction) is often intact (22). Similar to reports of Jax and colleagues (11) about the observed "conduit d'approche" in some patients, we also noted an increase in accuracy after multiple repetitions. Patients might have visually recognized their incorrect movements and tried to more closely approximate the correct action represented by the animated holograms.

Limitations

The psychometric properties of the applied Presence questionnaire (43) have not yet been validated in the stroke population or in patients with cognitive limitations. Unfortunately, eight patients failed to fill in the questionnaire, which indicates that it may not be the best measure to assess presence in this population. Besides a need of alternative questionnaires, the integration of objective measures (e.g., eye movements) is worth further investigation. In HoloLens 2nd generation, the feature of eye-tracking is incorporated offering an easy way to analyse visual attention based on eye movements, to assess salience and to identify the user's intention (35) and areas of interests (23). Indeed, while spatial attention is a major mechanism for saliency detection, patients with visuo-spatial or attentional deficits might not be able to focus their limited perceptual resources on the holograms. In this study, patients with a higher quality in stereovision had a higher DYN-Effect on the Production scale and a trend points toward an association of higher stereovision and interactions with animated holograms. We cannot rule out that some patients have been unable to see the holograms as intended and thus, have not benefited from its salient contextual information.

The technical presentation of realistic holograms also had its short-comings. In particular, some patients were unable to detect the key, possibly because it was displayed too close to the user and might have been overlooked because of not being visually distinct enough from its surrounding. On the other hand, participants criticized the holographic watering can appearing too far away in order to grasp for it, which was necessary to enable real-size presentations in the HoloLens. This illustrates the difficulty in finding the optimal zone for hologram positioning in experimental research, especially with the current technological limitations (e.g., limited field of view). The fact that the dynamic features had no significant impact on presence ratings may be due to these technological constraints (28).

The predefined eligibility criteria within the present study were quite broad. Consequently, we included patients in the subacute as well as in the chronic stage, patients with and without a diagnose of neglect, aphasia or cognitive decline, but did not adjust for these possible confounding factors. At the moment we are therefore not able to give differential recommendations to patients early and late after stroke. In addition, the effect of cues may have been underestimated in some patients if aphasia, neglect or attention deficits had deteriorated task understanding or stimulus perception. Further and in line with recent recommendations on post-stroke rehabilitation trials (58), we ensured an aphasia and neglect friendly testing (by following the DILA-S recommendations), which improved our recruitment rate and increases the generalizability of our results.

Outlook

Apraxia is a major predictor of poor functional performance in ADL and of increased dependence on caregivers. To date, effective rehabilitation strategies are still limited (9, 59) and mainly include compensatory approaches, such as strategy training (8, 60), errorless learning (61), behavioral training (62) or task-specific and meaningful training (63). In recent years, technology-based approaches facilitating single-tool use and multistep actions have been proposed as promising strategies (9, 64). AR technology has already found its way into a large field of applications, where holographic elements enrich the perception of the real environment, e.g., by providing cognitive support during different tasks (65). In the wide field of rehabilitation, AR will introduce new pathways for therapeutic or assistive approaches with the potential of providing an engaging and motivating training environment (31), improving physical outcomes when applied as an adjunct therapy (29), supporting mental rehabilitation (44) or cognitive rehabilitation (57, 66). Based on our findings, we envision HMD-based AR systems to assist patients in their ADLs in the future, thus maintaining autonomy. The advantages of wearable cognitive support systems over existing screen-based approaches (66, 67) are having both hands available for interactions with the physical environment while still being able to move flexibly from one place to another. In this regard, we see two main application areas where AR can be used: (1) as a supportive training tool to facilitate performance improvement and (2) as a (well-controllable) diagnostic research tool to further examine the role and importance of different modes and types of visual cues and to identify predicting variables.

While we showed that holograms can attract attention (e.g., by being visually salient) and improve performance, they can potentially also distract from the real activity and may require voluntary effort to redirect the attention to the physical objects (36). The objects within this study were displayed in a left handed setting (**Figure 2D**) and the holographic cues were aligned in space to invite the participant to reach for it as it was shown that the perception of affordances (here the orientation of the tools in space) influences the motor response that is best suited for interacting with the target object (23, 56, 68). In future trials on real tool support however, we recommend to place cues in a non-reachable zone because no interaction with holographic but rather real objects is desired. Besides, AR supported manual task guidance inside the peripersonal space is associated with vergence-accomodation-conflict (e.g., when the virtual content is inconsistent with the real world) and focus-rivalry (e.g., when simultaneously focusing on real and virtual content). These common perceptual conflicts experienced in artificial environments may impair the performance due to visual fatigue and mental workload, especially with increased task difficulty as recently suggested by preliminary data on EEG recordings during AR use (69).

Future experiments should investigate whether a further increase in visual fidelity and contextual information will lead to even better results (e.g., by adding the target item or illustrating a holographic hand correctly performing the action). Indeed, findings from a recent eye-tracking study analyzing the visuo-perceptual context within a virtual scene show that thematically consistent object-tool pairs (e.g., hammer and nail) can have a facilitating influence on visual attention (23). In addition, audio-visual complexity does provide opportunities to enhance individual meaning, salience and authenticity (70–72).

CONCLUSION

This study was the first to explore the effect of dynamic holographic cues on pantomiming in LBD patients. We provide first knowledge about which type of AR cue might be most beneficial in supporting patients with apraxia, present current limitations and give suggestions for further research. Specifically, studies are necessary to characterize the conditions that lead to optimal motor behavior in augmented environments, and to identify responders and factors that increase the potential effects of this new form of support. With further technological achievements (65) we believe this new approach to positively impact the rehabilitation process of patients with apraxia.

DATA AVAILABILITY STATEMENT

The datasets generated for this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: Center for Open Science (COS) Open Science Framework (OSF), https://osf.io/uakw2/?view_only=a55698fafb6541f7878284bab64e940c.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of the Medical Faculty of the Technical University of Munich (reference number 175/17S). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

NR and JH: conceptualization, methodology, and formal analysis. NR and AT: software and visualization. NR and LL: validation. NR, LL, and KJ: investigation. NR: data curation and writing – original draft preparation. CK, JR, KJ, and JH: writing – review & editing. CK: project administration. CK and JH: supervision. JR, KJ, and JH: resources. NR, CK, and JH: funding acquisition. All authors contributed to the final draft of the manuscript, read, and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.711900/full#supplementary-material

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Chapter 4

General Discussion

4. General Discussion

The number of people living with chronic neurological impairments and associated long term care is increasing. Consequently, there is an urgent need for innovative rehabilitative strategies to support restorative processes in the brain and to promote compensatory strategies for independent living (Stinear et al., 2020). This thesis investigated MR as a potential digital therapeutic approach for patients suffering from action disorders due to neurological disorders. We made use of AR technology as a unique way 1) to provide non-obtrusive guidance in real life tasks, and 2) to study basic underlying cognitive mechanisms, such as the factors that drive the SWI phenomenon and the impact of visual feedback on apraxia. Specifically, the goal was to determine the usability of an HMD-based AR device as an AAL system and to generate knowledge about the optimal display of virtual information. In addition, the available evidence about a user´s affective state in virtual environments and its influence on motor learning outcomes was studied. The following section provides a summary of the main results alongside a general discussion on virtual cueing and action guidance in neurorehabilitation, including suggestions for further research.

4.1 Virtual cueing and action guidance

The implementation of external cueing systems in neurorehabilitation that are designed with the purpose of inducing the user to perform a specific motor activity (Pérez et al., 2009), is a promising way to improve motor learning in patients with motor disorders (Palacios-Navarro et al., 2016). The use of external stimuli, such as visual, auditory, somatosensory or mixed cues, has been primarily studied for gait training in Parkinson´s Disease (Al-Issa et al., 2012), but has gained increasing attention in other domains, such as in the context of action guidance and assistive technology for patients with cognitive disorders (Funk et al., 2015; Wolf et al., 2019).

The Therapy Lens project (study II, p.24) aimed to implement and test the feasibility of a step-by-step guidance system for patients with forms of dementia and apraxia (Rohrbach, Gulde, et al., 2019). We hypothesized that an AR-based support system can function as a unique way to provide non-obtrusive multidimensional cues and as such, improve ADL task performance (such as tea making). We found that the applied system affected the users performance. Patients took significantly longer to complete the task compared to the control condition. Moreover, 30% of patients failed the task when making use of the system. We attributed this performance degradation primarily to the fact that the new application was a secondary task that required its own resources (i.e., higher cognitive demands). We provided several reasonable explanations for prolonged task durations and failure, including **personal conditions**, **hardware-related features** and **design principles** (see discussion in (Rohrbach, Gulde, et al., 2019)). Interestingly, a multiple linear regression analysis of prolonged time durations revealed that patients with more severe problems in executing the natural task showed lower increases in trial durations in the AR-condition. This indicated that dual task costs as a consequence of dealing with the application were almost balanced by the given support. Thus, we concluded that the system may be more beneficial for patients with a higher degree of impairment. One possible explanation could be that the more impaired patients have already developed acceptance for external assistance and instructions (e.g., from family members) (Meiland et al., 2017). For future implementation projects, a thorough familiarization phase is key, i.e., longer practice trials or even training with video demonstrations (Wolf et al., 2019), as this is expected to positively influence the overall task completion time.

4.1.1 Complexity of virtual feedback

The observed prolonged task durations were consistent with the findings of related research (Funk et al., 2015; Wolf et al., 2019). Wolf et al. (2019), implemented a HoloLens based AR framework ("cARe") that was developed to guide geriatric patients with cognitive decline in a cooking task (i.e., pancakes). The study found that the average cooking time was higher in the cARe condition, which was related to the detailed number of intermediate steps designed for a population with higher cognitive impairment than the patients enrolled in the study (Wolf et al., 2019). In contrast, in our Therapy Lens study, the implemented number of steps seemed to be insufficient and as such confused participants due to lacking details (Rohrbach, Gulde, et al., 2019). These findings highlight the difficulty in determining the optimal level of support for patients with heterogenous symptoms and the need for individualized systems.

Funk et al. (2015) explored different visualizations of augmented instructions within a projector-based system to assist mentally impaired workers in a manual assembly workplace. While best results were achieved with simple contour visualization (i.e., contouring of the position and orientation of a tool, usage of light or pointing arrows to highlight certain parts and actions) they observed an increase in time and error rates in the graphically more complex visualizations (i.e., video projections of actions) (Funk et al., 2015). This could be due to the limited capacity of people with cognitive impairement to process multidimensional feedback (e.g., in (Rohrbach, Gulde, et al., 2019)) or complex visualizations (e.g., in (Funk et al., 2015)). Hence, this patient group may benefit from cues of simplified complexity, i.e., unimodal and less multifaceted cues. On the other hand, the qualitative data supporting our Therapy Lens study suggest that the use of multidimensional cues was valued by the participants. In fact, the provision of multimodal support may facilitate the use of the system for a broader patient population with heterogenous symptoms and comorbidities, such as vision or hearing problems, attentional deficits or neurological impairments (e.g. aphasia) (Rohrbach, Gulde, et al., 2019). In addition, practicing in an enriched environment is expected to enhance learning (Lohse et al., 2016), which would support the use of multidimensional and complex stimuli. Research on the influence of VE audiovisual complexity on children`s motor learning, however, did not find any difference between simple vs. complex VE conditions (Levac et al., 2019). Based on these considerations, it is critical to characterize the conditions that lead to optimal cueing and action guidance in AAL and to identify the responders and factors that amplify the potential impact of this type of support.

To conclude, virtual cueing both facilitates and impedes task performance. On the one hand, the provision of virtual cues can be stimulating but also overwhelming for patients with cognitive decline, thus, the patient's attention is either drawn to or even dragged from the real task. On the other hand, a system may lack details to be sufficiently supportive and understandable, such as the number of steps or visual fidelity. We identified two key questions that need to be answered in order to successfully implement virtual cueing systems:

1. *How are holographic cues perceived and integrated into motor performance?*
2. *Which is the most efficient way in delivering virtual information for patients with action disorders?*
    - 2.1.1 *Are HMD-based systems actually superior to screen-based systems?*
    - 2.1.2 *Which are the relevant attributes of virtual cues to evoke an otherwise lost motor program?*

4.1.2 Sensorimotor integration of holographic cues

To address these questions and investigate the sensorimotor integration of AR cues, further experiments were conducted in which the visual-perceptual context was altered by AR. By designing the augmented SWI paradigm and focusing on healthy young individuals, we found an objective way to investigate the perception and sensorimotor integration of holographic cues during real object interactions (study III, p.28). The results were remarkable in that they showed that holographic cues to an object´s volume can initially even dominate physical cues and cognitive knowledge in unimpaired people, eliminating an otherwise robust perceptual illusion. This was the case even though the participants were constantly informed about the current physical information. However, when the holographic cues were removed, participants interacted analogously to the control group as if they had never experienced the artificial cues, indicating no learning or carry-over effect. These findings help to better understand the factors that drive the SWI, including the importance of visual cues. Even in the case that holographic cues merely distracted participants due to the novelty effect, the findings are of considerable importance for the design of assistive technologies as they provide evidence that holographic cues can stimulate interactions in the real environment. In fact, AR cues might be favorized over physical cues for a period of time. However, the results need to be confirmed in neurological populations as the perception and integration of virtual cues may vary greatly in different populations. For instance, the findings of the “Augmented Pantomime” trial (study IV) suggest that non-impaired individuals are more likely to interact with holograms. *Interaction* in this context has been defined as any attempt to reach for or grasp a hologram and in turn depends on different factors, such as the **individual conditions** of a human and the **characteristics of the virtual cue** itself. As such, patients with a higher quality in stereovision may benefit more from dynamic cues and may interact more with animated holograms. The results of the SPiAR study (Höhler et al., 2021), in which we followed up on this question, confirmed that impaired visuospatial perception in stroke patients can influence the perception within the augmented environment, e.g., the ability to correctly judge distances. In addition, patients with different cortical lesions seemed to rely on different cues (Höhler et al., 2020). These results indicate that sensorimotor processing of virtual stimuli depends on personal factors and design principles, and highlight the need for personalized systems.

4.1.3 Environment dependent characteristics of virtual cues

The goal of the final “Augmented Pantomime” trial (study IV) was to investigate the role of visual feedback on apraxia post-stroke and to unpack the relevant attributes of virtual cues (i.e., dynamic vs. static). In addition, we aimed to disentangle the relationship with user affect (i.e., sense of presence), the virtual environment (i.e., screen vs. HMD) and performance outcomes (i.e., pantomime of tool use). The rationale behind the experiment was based on previous research in patients with apraxia, highlighting the role of the visuo-perceptual context, object affordances and visual attributes within tool use (Federico & Brandimonte, 2019; Hermsdorfer et al., 2012; Hermsdorfer et al., 2013; Jax et al., 2014; Jax et al., 2006; Randerath et al., 2011). We hypothesized that more salient and realistic cues, such as dynamic holograms visualizing the intended use of tools (e.g., a striking hammer), would influence impaired movement execution in apraxic patients (Rohrbach, Krewer, et al., 2021). The results of our study revealed a significant improvement in a pantomime of tool use task with the help of *dynamic* or *holographic* cues. In fact, the pantomime performance appeared more equivalent to the real tool demonstration when being supported by *dynamic holograms*, supporting the use of HMD-based systems over screen-based systems. Moreover, the performance improved significantly with increased presence ratings within the HMD^{Dyn} condition (i.e., dynamic holograms), highlighting the importance of affective state in virtual environments.

4.2 The importance of affective state in virtual environments

Although currently available technological systems, such as VR interventions in motor rehabilitation post-stroke seem to be beneficial as an adjunct to usual care (Laver et al., 2017), they are, to date, not superior to conventional approaches (Stinear et al., 2020). Essential challenges in neurorehabilitation settings are to keep patients motivated and engaged in therapy as well as in their home environment and to maintain adherence. The conducted scoping review as part of this dissertation (study I, p.21) aimed to elucidate the role of affective factors in virtual environments and how they may contribute either indirectly (e.g., via increased dosage) or directly (e.g., via altered hormone release) to motor learning. A holistic overview of the active ingredients in virtual rehabilitation, irrespective of the utilized technology, will contribute to better understand their added value in post-stroke rehabilitation and can inform the design of more effective VR interventions (Darekar et al., 2015; Doumas et al., 2021; Maier, Rubio Ballester, et al., 2019). To this end, the goal was to explore how VR/AVG studies measured or reported client enjoyment, motivation, engagement, immersion and presence, and further evaluate the potential links between these five constructs and motor learning outcomes. The results reflected the growing interest on the role of affective state in learning. Almost 90% of the included studies mentioned at least one of the five constructs, either as a rational for VR/AVGs use or as an explanation for their intervention results. However, inconsistencies in definitions, terminology, and measurements limited conclusions (Rohrbach, Chicklis, et al., 2019). Indeed, measurements were undertaken only within 32% of included studies, and assumptions about multiple relational links were only hypothesized – often even stated as facts – but not confirmed by statistical analyses. These findings highlight the need to better understand and measure whether these constructs contribute to motor learning outcomes (Rohrbach, Chicklis, et al., 2019).

4.2.1 Transfer of knowledge to HMD-based AAL systems

The knowledge derived from the scoping review can also inform future research activities on AR based training tools or assistive technologies for patients with motor-cognitive impairments. The affective state is also likely to influence the use and acceptance of assistive devices. After all, the execution of daily tasks is determined by our motivational states, e.g., our thirst drives us to prepare a cup of tea (Frey et al., 2011). However, brain changes that occur in patients with AD can impair fundamental abilities necessary to prepare a drink (see 1.2.2 Dementia of the Alzheimer's type). As the disease progresses, patients often forget to be thirsty, thus, requiring support from caregivers who remind them to stay hydrated. A well-designed support system could be an alternative solution to preserve autonomy. The missing but vital intrinsic motivation to take care of oneself and to focus on fundamental activities could be compensated by providing extrinsic motivation in the form of external cues and support in an enjoyable fashion, which was also suggested by one of our participants in the Therapy Lens trial (study II). The hypothesis that task performance can not only be directly influenced by the provision of visual cues (e.g., achieving the goal by means of augmented information), but also indirectly through the affective state of the patient (e.g., achieving the goal by externally motivating the patients in their action planning process) has to be further explored. In summary, findings from studies in virtual environments cannot simply be transferred to augmented environments, because different technological systems differ, e.g., in the level of immersion and induced sense of presence.

4.2.2 Sense of presence in augmented environments

The elicited sense of presence varies across environments and is likely to be more pronounced in augmented environments than in virtual environments (Regenbrecht & Schubert, 2002). An increased sense of presence can influence user effects (e.g., the extent to which a user interacts with virtual stimuli) which can in turn increase the effectiveness of the application (e.g., training effect) (Cummings & Bailenson, 2016). In line with this argumentation, graphically more complex presentations of objects may only increase the sense of presence within an HMD environment but not within screen or projection-based environments. This may explain why results of the “Augmented Pantomiming” trial (study IV) support the implementation of more complex stimuli in HMD environments (i.e., dynamic holograms), whereas Funk et al. (2015) obtained the best results with simple contour-based cues in their projection-based system. Assessing the evoked sense of presence while using assistive systems (such as the Therapy Lens system (Rohrbach, Gulde, et al., 2019) or (Funk et al., 2015), and linking these results to the performance duration and errors, could provide further insight into how the virtual cues are perceived, e.g., as being real, spatially present or whether they provoke any perceptual stress in users.

Apart from this, presence in augmented environments conveys a sense of “being here” rather than “being there” as in virtual environments (Regenbrecht & Schubert, 2002). Studies suggest that practicing in a familiar context, such as the home environment, supports task performance for patients with apraxia (Bieńkiewicz et al., 2014; Geusgens et al., 2007). We conclude that the characteristic of being still *present* in the real environment is an essential component for rehabilitative purposes in patients with cognitive impairments and action disorders. Once patients with AD have difficulty recognizing familiar objects or people, it may become essential to keep them present in reality rather than immersing them in a completely virtual world, supporting the use of unobtrusive AR-based HMDs over closed VR-based HMDs.

4.3 Conclusion & Outlook

The results of the four studies encompassing this dissertation show that MR technology can be a powerful tool to 1) impact the affective state, 2) influence task performance, and 3) drive interactions in the real environment, in both, healthy individuals and patients. These findings have significant theoretical and applied implications for sensory combination, technological properties (e.g., salience) and user attributes (e.g., sense of presence) in mixed environments and may inform the development of assistive technologies for motor-cognitive rehabilitation. Based on the presented findings, HMD-based AR systems should be considered as an assistive technology to support patients with action disorders in their daily life activities, with the advantages of 1) providing non-obtrusive feedback, 2) still allowing users to have a natural view on their physical environment, 3) having both hands available for manual interactions, and 4) allowing users to move from one place to another. The following factors were identified key for a successful implementation of MR-based assistive technologies, because of their impact on the perception of and response to virtual cues:

- **Personal conditions.** The presence of neurological symptoms, e.g., action disorders, may affect the perception of holograms and the way to interact with them. People with attentional, visuo-spatial or cognitive deficits might not be able to focus their limited cognitive resources on holograms (Rohrbach, Gulde, et al., 2019) or to accurately perceive distances and three-dimensionality in augmented environments (Höhler et al., 2020; Höhler et al., 2021), and thus, might not be able to make use of the intended support. Specific disorders, such as apraxia, aphasia or neglect can further deteriorate stimulus perception (Höhler et al., 2021; Rohrbach, Krewer, et al., 2021).
- **Hardware-related features.** The hardware itself can influence the wearing comfort and as such, the level of acceptance and satisfaction. Technological limitations (e.g., a limited field of view) can influence the AR-experience and user affect (Rohrbach, Gulde, et al., 2019).
- **Design principles.** Decisions about the design of virtual cues (simple vs. complex, contour-based vs. realistic, static vs. dynamic, pointing arrows vs. complex videos), the positioning (non-reachable vs. reachable zone) and presentation of virtual cues (static vs. dynamic, first person perspective vs. third person perspective) and complexity of feedback (unimodal vs. multimodal) are de-

pendent on the user and the environment and will influence performance outcomes, user affect and satisfaction (Funk et al., 2015; Levac et al., 2019; Rohrbach, Krewer, et al., 2021; Wolf et al., 2019).

- **Virtual environment.** The perception of virtual attributes, e.g., audiovisual complexity, differs between screen-based, projector-based, and HMD-based systems and impacts user performance and affect. The likelihood of experiencing side effects, such as motion sickness or perceptual conflicts (e.g., vergence-accommodation-conflict, focus-rivalry) varies depending on the environment and the personal conditions.
- **User affect.** Factors, including motivation, enjoyment, engagement, immersion and presence contribute to motor learning in virtual environments (Rohrbach, Chicklis, et al., 2019). Software-related features (e.g., audio-visual complexity) can influence user affect (e.g., motivation or fun) (Levac et al., 2019).

Current healthcare systems fail to deliver high-quality, evidence-based interventions (e.g., early, high intensity, high dose training) and access to rehabilitation programs is limited and depend on the patients´ socioeconomic status (Choi et al., 2019). In addition, most patients with neurological disorders do not receive follow-up treatment and often become dependent on caregivers. Digital therapeutics can provide a high-quality, cost-beneficial solution to the challenges in neurorehabilitation by offering high intensity training and home-based solutions. AAL systems using HMD-based MR technology seem feasible and usable for patients with motor-cognitive disorders and thus, have the potential to make a significant contribution to supporting people with action disorders in their home environment. To advance the development of assistive devices and make them applicable for non-experimental settings, studies are needed that characterize the conditions that lead to optimal motor behavior in augmented environments identify the factors that increase the potential effects of this type of assistance. Above all, the system must be personalized because both the patient´s state (e.g., personal condition, affective state) and the way of delivering cues (e.g., virtual environment, hardware, design principles) highly influence the task performance. For future deployments, the ultimate goal is to develop action recognition systems that automatically detect errors and provide real-time assistance only when needed. In addition, new models of care must be initiated to make available therapeutic approaches accessible to patients and to facilitate a science-practice transfer for the benefit of the general public.

Affidavit

I hereby confirm that the dissertation „Mixed Reality as a new rehabilitative approach to assist activities of daily living in patients with chronic neurological disease" is the result of my own work and that I have only used sources or materials listed and specified in the dissertation.

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Appendix

Codebook – Step by Step – Crossover Study

Code	Summary
Others	Degree of severity affecting the data collection: Patient can´t remember any of the cues – can´t give feedback --> because he failed to fulfill task, didn't understand the concept Patients\P14_Cycle 4 (5)
Ethical considerations	Overreliance on technology: in TM-condition patient was not able to fulfill task because he "stopped thinking", he did not put the kettle on the socket so the water could not heat up Patients\P5_Cycle 4 (3)
	Disempowerment; doesn´t like it that much because knows everything Patients\P11_Cycle 4 (2)
	New risks: accident prevention has to be considered! In case someone slips over a cable Fear for replacement or loss of human contact? Patients\P17_Cycle 4 (8)
Ethical considerations\ Description of TL app	Information given on single steps: when you fulfill one step than this one is done Patients\P5_Cycle 4 (3)
	Didn´t enjoy the communication with the TL because she can do it on her own Patients\P11_Cycle 4 (2)
	Describes experiences as unusual, because has never done it before; very new, one needs time to orientate and time to build opinion on whether it is useful for on or other people Patients\P16_Cycle 4 (7)
	Step by Step: describes it as an exercise, (...) with announcement and (...) yes, it did not have any influence on his inner condition and yes, I hope, everything worked (laughs) Patients\P18_Cycle 4 (9)
	Experienced Step by Step as very interesting; system told what to do next, and caught attent Patients\P19_Cycle 4 (10)
Potentials - Facilitators\ Usability\Hardware related facilitators	+ Describes the HoloLens as being "not uncomfortable" and light weighted Patients\P10_Cycle 4 (1)
	Speaking function is valued Patients\P11_Cycle 4 (2)
	Wearing comfort: + "It is very light weighted. One has to say." Patients\P12_Cycle 4 (4)
	Wearing comfort: + HoloLens fits pretty well; even when head is moved they do not slip – can imagine wearing it at least 1 hour, even 2, if needed longer. + Experienced the glasses as being leigh weighted Patients\P15_Cycle 4 (6)
Potentials - Facilitators\ Usability\Technique related facilitators	Command: Cue "next" seemed to work for him; he suggested "next step" as another cue Patients\P5_Cycle 4 (3)
	Cueing: + Prefers the hologram because pictures can be stored. + multiple cues were not experienced as being uncomfortable Command: + Cue "weiter" worked well Patients\P10_Cycle 4 (1)
	Cueing: + text might be useful but not everybody can read Patients\P11_Cycle 4 (2)

	Layout Text: + Readability "gut lesbar" Layout Audio: + Clear audio instructions; easily audible; Pleasant voice Command: + Cue "weiter" worked very well Patients\P12_Cycle 4 (4)
	Cueing: + Prefers audio over text as it is better noticed Patients\P14_Cycle 4 (5)
	Layout Text: + well readable, good instruction; prefers text over audio because can´t hear very well Patients\P15_Cycle 4 (6)
	Cueing: + prefers holograms out of all options, because you can react immediately and would not confuse anything as with text where you have to read first "a picture is a pictur Patients\P16_Cycle 4 (7)
	Cueing: + Prefers to have both, audio + text because of vision or hearing problems in the elderly; or option of individualizing it Patients\P17_Cycle 4 (8)
	Researcher only asked about audio and text (not holograms): patient prefers having both cues rather than one, to avoid misunderstandings, to be sure Patients\P18_Cycle 4 (9)
	Cueing: + Describes cues during step by step as clear + Seems to prefer audio; valuables audio cue because otherwise she might have performed an error in the execution of the task Patients\P19_Cycle 4 (10)
Potentials - Facilitators\ Usability\Usefulness & effectiveness & acceptability	Believes he understands Patients\P10_Cycle 4 (1)
	- liked it, but wouldn´t use it Patients\P12_Cycle 4 (4)
	Experiences testing as meaningful - needed for research; influenced by testing procedure – believes "it is for a good purpose" Patients\P18_Cycle 4 (9)
Potentials - Facilitators\ Usability\Usefulness & effectiveness & acceptability\ Motivational factors	Fun: Maybe it's good to put a fun factor in it, because if it's always so real and serious then you're a bit scared or then. Well, fun, of course, is difficult with such a story. Patients\P5_Cycle 4 (3)
Potentials - Facilitators\ Benefits of technological support system\ Therapy Lens specific	Good help in orientation which step is next Patients\P5_Cycle 4 (3)
Potentials - Facilitators\ Benefits of technological support system\ Needs/further ideas/ suggestions ADL´s	Forgetfulness: cant remember where he put things, e.g. glasses which drives him crazy, spent hours in the past to find things he put somewhere he could not remember anymore Patients\P5_Cycle 4 (3)
Challenges - Barriers\ Usability\ Technique related barriers	Lack of Structure: Missing cue - Patient did not know when step was finished (water boiling), what to do next Lack of Structure: missing cue - Patient didn´t put kettle on the socket, so it could not start to boil even though he switched on the kettle successfully Patients\P5_Cycle 4 (3)