

Université Catholique de Louvain

Psychological Sciences Research Institute (IPSY)

Institute of Neuroscience (IoNS)

Advances in the diagnosis and neurorehabilitation of spatial neglect and distractor inhibition impairments using XR

Gregorio Sorrentino

Thesis submitted in fulfilment of the requirements for the degree of

“Doctor of Medical Sciences”

Supervisors: Martin Edwards & Thierry Lejeune

June 2026

Jury

Chair:

Professor Valéry Legrain

UCLouvain, Belgium

Supervisors:

Professor Martin Edwards

UCLouvain, Belgium

Professor Thierry Lejeune

UCLouvain, Belgium

Jury Members:

Professor Gilles Rode

Université Claude Bernard, Lyon 1, France

Professor Brigitte C. Kaufmann

University of Lucerne, Switzerland

Professor Céline Gillebert

KU Leuven, Belgium

Professor Bernard Hanseeuw

UCLouvain, Belgium

Table of contents

Jury	3
Table of contents.....	5
Summary	7
Résumé.....	7
Chapter 1 - General Introduction	9
Stroke	9
Spatial attention and distractor inhibition.....	10
Serious games and virtual reality as assessment tools	14
Beyond behavioral outcomes: Toward process-oriented assessment	15
The role of immersion in cognitive processing	16
From assessment to adaptive cognitive rehabilitation.....	17
Objective of the present PhD thesis.....	21
Structure of the thesis.....	23
Chapter 2 - A non-immersive virtual reality serious game to assess distractor inhibition and spatial target selection on response time attention in post-stroke individuals	25
Chapter 3 - The REAsmash serious game for the post-stroke diagnosis of distractor inhibition: Contrast between immersive and non-immersive virtual reality test versions.....	57
Chapter 4 - REAsmash-ET: A methodological framework for combined cognitive and motor assessment through eye-tracking and kinematic metrics in immersive VR search-and-reach task	85
Chapter 5 - Feasibility of a theory-driven dynamic difficulty adjustment algorithm integrating individual performance and normative data for adaptive modulation of spatial and distractor inhibition attention in a non-immersive virtual reality task: Evidence from individuals following Stroke.	151
Chapter 6 - General Discussion	193
Reframing assessment in VR: from tasks to systems	193

Stability of paradigms and the role of immersion (Chapters 2 and 3)	195
ET in VR: from measurement transfer to methodological adaptation (Chapter 4)	196
From assessment to adaptation: toward dynamic task regulation (Chapter 5)	198
Thesis limitations and future perspectives	199
Conclusion	203
List of Abbreviations.....	205
Bibliography	207

Summary

Stroke frequently results in attentional impairments that limit functional recovery. Although virtual reality and serious games have shown potential for cognitive assessment and rehabilitation, current approaches remain limited in their ability to characterize underlying attentional processes and to individualize rehabilitation. This thesis presents the development of the REAsmash framework to improve the assessment and rehabilitation of post-stroke spatial and non-spatial attentional impairments using extended reality technologies. Across four studies, REAsmash evolved from a serious game assessing spatial attention and distractor inhibition to an integrated framework combining immersive virtual reality, eye-tracking, upper-limb kinematics, and adaptive rehabilitation through a theory-driven dynamic difficulty adjustment algorithm. Overall, this work supports the feasibility of using XR technologies to provide more sensitive assessment and individualized cognitive rehabilitation following stroke.

Résumé

Les accidents vasculaires cérébraux (AVC) entraînent fréquemment des troubles attentionnels limitant la récupération fonctionnelle. Bien que la réalité virtuelle et les jeux sérieux aient montré un potentiel pour l'évaluation et la rééducation cognitives, les approches actuelles restent limitées dans leur capacité à caractériser les processus attentionnels sous-jacents et à individualiser la rééducation. Cette thèse présente le développement du projet REAsmash afin d'améliorer l'évaluation et la rééducation des troubles attentionnels spatiaux et non spatiaux après AVC à l'aide des technologies de réalité étendue. Au travers de quatre études, REAsmash a évolué d'un jeu sérieux évaluant l'attention spatiale et l'inhibition des distracteurs vers un instrument intégré combinant réalité virtuelle immersive, suivi oculaire, cinématique du membre supérieur et rééducation adaptative. Dans son ensemble, ce travail démontre la faisabilité d'utiliser les technologies XR pour offrir une évaluation plus sensible et une rééducation cognitive individualisée après AVC.

Chapter 1

General Introduction

Stroke

Approximately 80 million individuals worldwide live with the consequences of stroke, a leading cause of long-term disability in developed countries, and ranking among the top causes of disability-adjusted life years globally^{1,2}. In the last decade(s), predictions have been made for a 35% increase in prevalence by 2030^{3,4} (relative to 1990 and 2020). These projections have further reinforced the need for research on stroke, including the development of innovative approaches to diagnosis and neurorehabilitation.

Following stroke, spontaneous recovery occurs, driven by mechanisms of cerebral plasticity⁵. This process of spontaneous recovery is most pronounced during the early post-stroke phase and tends to decrease over time with a plateau reached between 6 months and one year after the stroke onset^{6,7}. Accordingly, intensive rehabilitation is recommended as early as possible after stroke to capitalize on this recovery process, and further, it is recommended that rehabilitation should be tailored to the individual patient's profile of impairments to support neuroplasticity and maximize recovery⁸. However, despite these recommendations, rehabilitation pathways remain heterogeneous across clinical settings, and ensuring a comprehensive, individualized, and needs-oriented approach continues to represent a major challenge, even in high-income healthcare systems^{9,10}.

In clinical practice, rehabilitation pathways tend to be primarily structured around motor recovery¹¹. This focus is justified, as motor impairments are the most frequent, readily observable and quantifiable, and directly linked to autonomy¹². However, recovery of motor function alone does not necessarily predict effective functioning in real-world daily life¹³. Many

Chapter 1 - General Introduction

stroke survivors who regain satisfactory strength, articular range of motion, balance, and gait, may still experience disabling difficulties in everyday situations¹³. These difficulties include locating objects, interacting efficiently with multiple elements, navigating space, or completing goal-directed actions in dynamic contexts¹⁴. Such difficulties are particularly evident in situations requiring the integration of perception, attention, and action¹⁵. Stroke survivors may also experience difficulties in socially complex environments (e.g., crowded or new places) or during cognitively demanding activities, such as interacting with multiple individuals simultaneously¹⁶. These persistent limitations, largely related to cognitive impairments, can lead to frustration, reduced participation, and social isolation further compromising quality of life^{17,18}.

Among cognitive impairments, attentional dysfunctions play a central role in recovery, as they influence the selection and integration of sensory information, thereby shaping how individuals explore, interpret, and respond to their environment¹⁴. As a result, attentional impairments affect motor performance, motor learning, and social interaction, and may explain why rehabilitation strategies focused solely on motor recovery often fail to address key determinants of functional recovery^{16,18,19}.

Spatial attention and distractor inhibition

Unilateral Spatial Neglect (USN) is one of the most frequent and disabling cognitive consequences of stroke, particularly following right hemisphere lesions^{20,21}. It is consistently associated with longer rehabilitation stays, poorer functional outcomes, and reduced independence²⁰.

USN is classically defined as a failure to report, respond, or orient to stimuli presented in contralesional space, which cannot be explained by primary sensory or motor deficits²¹. Although USN is frequently referred to as a single clinical syndrome in the literature, it encompasses multiple partially dissociable clinical subtypes. From a behavioral perspective, USN may be classified as perceptual, motor, or representational²². Perceptual USN refers to reduced awareness of contralesional stimuli in space or the contralesional

side of stimuli (egocentric versus allocentric perceptual USN) despite preserved primary visual sensory functions. Motor USN is characterized by reduced spontaneous use of the contralesional limb or reduced exploration and motor kinematic misreaching to objects in contralesional space despite being able to see the target object and having relatively preserved motor capacity that cannot explain the motor impairments²³. Representational USN reflects contralesional impairments in processing of internally generated mental representations, indicating that USN may affect both perceived and imagined (remembered) space²⁴.

USN can also be classified according to the spatial domain involved, affecting personal space (the patient's own body), peripersonal space (within reaching distance), or extrapersonal space (beyond arm's reach)²². These manifestations may occur independently or coexist within the same individual, reflecting the multidimensional nature of the syndrome²². Furthermore, the severity and clinical presentation of USN also depend on the location and extent of the brain lesion, as different components of the attentional network and their white matter connections may be selectively disrupted²⁵. Among these manifestations, peripersonal visual neglect is the most extensively investigated subtype^{22,25} and constitutes the primary focus of the present thesis. Focusing on a single, well-defined subtype also provides a methodological advantage by reducing the heterogeneity associated with different manifestations of USN, thereby enabling a more controlled investigation of the relationship between spatial attention deficits and inhibitory dysfunction. However, this approach also limits the generalizability of the findings. Consequently, the results presented in this thesis cannot be assumed to extend to other forms of neglect, such as personal or extrapersonal neglect, and future studies will be required to determine whether similar patterns of inhibitory impairment are observed across these subtypes. USN has been interpreted through several complementary theoretical frameworks that explain different aspects of the syndrome. Rather than representing competing hypotheses, these models describe neglect at different levels, ranging from cognitive mechanisms of attentional orienting to hemispheric specialization and large-scale brain networks.

Chapter 1 - General Introduction

Posner's attentional orienting model conceptualizes attention as a sequence of three operations: (1) disengaging attention from a current location of focus; (2) shifting attention to a new location, and; (3) engaging attention to the selected new location^{26,27}. Within this framework, USN has been largely interpreted as a deficit in disengaging attention from ipsilesional stimuli, leading delayed orienting of attention towards contralesional space and causing the characteristic slowness to attend to locations in contralesional space^{26,27}.

Heilman's hemispheric activation model proposes that the right hemisphere of the brain plays a dominant role in directing attention toward both sides of space, whereas the left hemisphere of the brain primarily directs attention towards contralateral hemisphere²¹. Consequently, right hemisphere lesions produce an imbalance in hemispheric attentional control, resulting in reduced allocation of attentional resources toward contralesional space²¹. This model further emphasizes that USN extends beyond perceptual deficits, affecting both the selection of sensory information and the preparation of actions directed toward contralesional stimuli²¹.

More recently, Corbetta and Shulman proposed a network-based model in which visuospatial attention emerges from the interaction between the dorsal attention network, responsible for goal-directed attentional orienting, and the ventral attention network, involved in stimulus-driven reorienting toward behaviorally relevant events²⁸. According to this account, right hemisphere damage disrupts the functional balance between these networks, impairing attentional reorienting toward contralesional stimuli and contributing to the ipsilesional attentional bias observed in USN²⁸.

Together, these complementary theories that explain the mechanisms underlying the behavioural observations of USN may support the view that USN is not a unitary disorder but the consequence of interacting impairments affecting attentional orienting, hemispheric attentional control, and large-scale attentional networks²⁹.

USN is classically assessed using standardized paper-and-pencil

neuropsychological tests such as cancellation tasks (e.g., the Bells Test³⁰, the Broken Hearts Test³¹), line bisection³² and copying or drawing³³. These tests capture spatial asymmetries using simplified and static stimuli conditions, identifying USN through lateralized omissions or biases in responses³³. Computerized cognitive assessments extend paper-and-pencil tests by providing additional measures of processing speed, typically revealing lateralized differences in the time taken to respond to stimuli in contralesional relative to ipsilesional space³³.

Gold-standard cancellation and computerized tests for spatial attention share the common feature of presenting spatial targets among distractor stimuli that compete for attentional resources^{34–36}. The presence of distractors increases the sensitivity of these tests to spatial attentional deficits, as the successful identification of a target requires the inhibition of distracting stimuli³⁷. Although routinely used in clinical settings by neuropsychologists, these tests have limited motivational appeal, which may increase response variability, particularly in fatigued patients, and rely on simplified two-dimensional stimuli that poorly reflect real-life interactions^{33,38}.

The relevance of distractor inhibition, a non-spatial component of attention, extends beyond the assessment of spatial attention and has been increasingly recognized as an important mechanism supporting goal-directed behavior³⁷. During serial search, distractor inhibition enables the disengagement of attention from task-irrelevant stimuli and prevents attention from returning to previously inhibited distractors^{39–41}. Impairments in this mechanism lead to increased attentional capture and inefficient visual exploration, thereby compromising goal-directed behavior⁴². Critically, clinical tools allowing systematic assessment of distractor inhibition during visual search remain limited⁴³. Consequently, these impairments may be underrecognized, and their prevalence and functional impact remain insufficiently characterized among stroke survivors.

A major issue in routine clinical practice is that attentional functions are not systematically integrated into the core of rehabilitation pathways⁴⁴. While cognitive screening using the Mini-Mental State Examination (MMSE)⁴⁵,

Chapter 1 - General Introduction

the Montreal Cognitive Assessment (MoCA)⁴⁶ or Oxford Cognitive Screen (OCS)³¹ can identify preliminary cognitive impairments, there is often a lack of specialized personnel and organizational resources that can carry out comprehensive cognitive evaluation, even in developed healthcare systems^{47,48}. As a result, the cognitive dimension of post-stroke impairment is often only partially characterized and considered in neurorehabilitation settings, which may negatively affect overall recovery⁴⁸.

Beyond the initial evaluation, comprehensive assessment should not be considered a static, one-time procedure, but rather a dynamic and iterative process aimed at capturing change, detecting residual deficits, and guiding therapeutic adjustments⁴⁹. This is particularly relevant for cognitive functions, which are often less directly observable⁵⁰. An assessment framework that is sensitive, repeatable, and applicable across motor and cognitive domains is therefore essential to support individualized and adaptive rehabilitation protocols. These limitations highlight the need for assessment approaches capable of capturing attentional processes under repeatable, controlled, and functionally relevant conditions. This perspective is consistent with recent clinical guidelines^{8,12}, which emphasize the need for standardized, sensitive, and functionally relevant assessment strategies to guide individualized rehabilitation and monitor recovery trajectories.

Serious games and virtual reality as assessment tools

Serious games (SGs) are defined as interactive tasks designed with a primary purpose beyond entertainment⁵¹. By embedding task demands within structured and goal-directed activities, SGs can support engagement while preserving experimental control, thereby facilitating repeated and reliable assessment^{52–54}. Within this context, virtual reality (VR) provides the technological basis for implementing such interactive tasks within controlled and flexible environments⁵⁵. VR systems can be implemented at different levels of immersion^{56,57}. Non-immersive VR, which is conceptually close to computerized testing, presents tasks on standard displays or interactive surfaces, allowing controlled stimulus presentation and precise measurement of performance^{57,58}. In contrast, immersive VR

creates a surrounding three-dimensional environment, enabling interaction through natural head and body movements⁵⁹ by employing Large Projection Systems (LPSs), Cave Automatic Virtual Environments (CAVEs) or Head-Mounted Displays (HMDs)⁵⁹.

VR SG have been proposed as potential tools for delivering more effective, repeatable, and ecologically valid post-stroke assessment^{60,61}. The use of VR SG allows the creation of interactive simulated environments in which task demands can be systematically manipulated⁵². In addition, VR SG approaches support the integration of complementary data streams, such as gaze and movement recordings, offering a more comprehensive characterization of cognitive functioning^{62–64}. However, despite these potential new measures, currently, most SG approaches, including VR-based paradigms, rely primarily on behavioral outcomes such as omissions and response time, limiting the detail of understanding the underlying attentional processes.

In the present thesis, these technologies were implemented within the REAsmash SG paradigm (using immersive and non-immersive VR) to enable controlled and flexible investigation of attentional processes within structured interactive environments.

Beyond behavioral outcomes: Toward process-oriented assessment

By capturing behavior at a finer level of granularity, VR SG enables a more detailed characterization of cognitive and motor processes⁵⁵. In particular, eye movement and upper-limb kinematic recordings provide direct access to how individuals explore environments and interact with stimuli within environments^{60,65}.

Eye tracking (ET) provides continuous and objective measures of visual behavior by recording gaze position over time⁶⁶. Core metrics include fixation location and duration, reflecting where and for how long attention is allocated, and saccadic movements reflect index shifts of attention across space⁶⁷. In visual search tasks, these measures allow the reconstruction of exploration patterns, revealing how individuals select, prioritize, and revisit

Chapter 1 - General Introduction

stimuli within the environment⁶⁵.

The use of ET enables the investigation of attentional processes that are not accessible through reliance on the typical outcome measures of omissions and response time. For example, repeated fixations on the same stimulus may reflect difficulties in disengaging attention, while spatial biases in fixation distribution may indicate altered allocation of attention across the visual field^{68,69}. In this way, ET provides a process-oriented characterization of attentional dynamics, with fixation-based metrics offering direct insight into mechanisms such as attentional selection, competition, and disengagement⁶⁵.

Importantly, the growing accessibility of commercially available VR hardware and software, including HMDs, largely driven by the gaming industry, has substantially reduced costs and technical barriers⁶⁰. HMDs are wearable devices equipped with integrated displays and tracking technologies. In the present work, two distinct HMD configurations were employed: a commercially widespread standalone headset (Meta Quest 2[®] / Oculus Quest 2[®]) representative of the growing accessibility of immersive VR technologies, and a gaming-derived system (HTC Vive Pro Eye[®]) integrating embedded Tobii ET technology, enabling the acquisition of gaze-based behavioral measures⁵⁹. Their strong clinical utility relies on their portability, ease of use, and minimal setup requirements^{62–64}. This convergence facilitates the development of scientifically rigorous and technically reliable tools with familiar interfaces, thereby enhancing their potential feasibility for clinical use⁵⁹. However, although the number of studies on VR-based stroke rehabilitation is increasing, recent reviews indicate that the evidence remains heterogeneous and often limited by variable intervention designs, inconsistent outcome measures, and methodological weaknesses⁷⁰.

The role of immersion in cognitive processing

The various VR configurations differ not only in their technological characteristics but also in the way users interact with the environment. Non-

immersive VR systems provide a constrained and familiar interaction format, which may reduce task-irrelevant cognitive load and facilitate the isolation of cognitive processes⁵⁷. This format is conceptually comparable to conventional assessments, where responses are typically limited to simplified actions such as marking targets with a pencil in paper-and-pencil tests or pressing a button in computerized tasks⁵⁸. In contrast, immersive systems allow unrestricted exploration and direct interaction with three-dimensional objects, enabling more naturalistic behavior that may be closer to real-world functioning^{57,59}.

Despite their increasing use, direct comparisons of identical task paradigms across different levels of VR immersion remain scarce⁵⁸. Existing studies predominantly rely on behavioral outcomes obtained in either conventional tasks or virtual environments⁵⁸. As a result, it remains unclear whether performance measures obtained in immersive and non-immersive VR environments can be directly compared, and whether the core characteristics of a given task are preserved across different implementations. Understanding how immersion influences outcomes is essential for both fundamental research and the development of clinically relevant tools.

From assessment to adaptive cognitive rehabilitation

A more precise and process-oriented characterization of attentional deficits raises the question of how such information can be used to guide rehabilitation. In this context, current rehabilitation approaches for USN are typically divided into bottom-up interventions, which act on sensorimotor processes, and top-down strategies, which rely on voluntary control of attention⁷¹.

Given the heterogeneous clinical presentation of USN, multiple rehabilitation approaches have been developed targeting different cognitive and sensorimotor mechanisms. These interventions are commonly classified into relearning (restorative) approaches and compensatory approaches, the latter relying either on internal cognitive strategies or external aids to reduce spatial bias.

Chapter 1 - General Introduction

Among relearning approaches, prism adaptation is one of the most extensively investigated interventions, as it relies on implicit sensorimotor recalibration driven by visuomotor error signals⁷¹. During the intervention, patients wear prism goggles that laterally shift the visual field while repeatedly performing visually guided pointing movements toward visual targets⁷². Initially, pointing errors occur in the direction of the optical shift, but repeated movements gradually reduce these errors through sensorimotor adaptation⁷³. Once the prisms are removed, a compensatory after-effect is observed in the opposite direction, reflecting recalibration of visuomotor coordinates^{74–76}. Although this adaptation is driven by low-level sensorimotor processes, its effects extend to higher-level spatial representations, contributing to a reduction of the pathological ipsilesional spatial bias characteristic of USN⁷¹. In recent years, it is one of the most extensively investigated rehabilitation approaches for USN and has consistently demonstrated short-term improvements on standardized neuropsychological assessments^{77,78}. However, the mechanisms underlying these improvements and the extent to which they generalize to everyday activities remain subjects of ongoing investigation⁷⁷. Relearning approaches also include paradigms based on repeated practice of goal-directed visuospatial exploration⁷⁹. In these interventions, patients are repeatedly required to detect and identify visual targets while external cues, feedback, or task manipulations facilitate orienting toward contralesional space^{79,80}. Through repeated exposure and practice, these paradigms aim to progressively recalibrate attentional allocation and reduce ipsilesional bias without relying primarily on explicit compensatory strategies⁸⁰. REAsmash builds upon this rehabilitation principle by embedding these relearning mechanisms within an adaptive serious game that continuously individualizes task difficulty according to the patient's ongoing performance.

Compensatory approaches based on internal strategies rely on the voluntary control of attention and the acquisition of compensatory strategies⁷¹. The most widely adopted intervention is visual scanning training, which encourages patients to systematically explore contralesional space through structured, task-specific exploration patterns^{71,81}. Additional approaches

include self-cueing techniques, visual anchors, and body-related cues designed to facilitate intentional orienting toward neglected space^{71,81}. Although these interventions can improve performance on trained tasks, particularly reading and paper-and-pencil assessments, transfer to more complex real-world activities remain variable and underinvestigated⁸¹.

Several additional rehabilitation approaches have been investigated, each targeting different mechanisms contributing to USN. Limb activation therapy aims to increase spontaneous movements toward the contralesional side, thereby facilitating spatial orienting through sensorimotor activation^{80,82}. Neck muscle vibration modulates proprioceptive input and is thought to transiently influence egocentric spatial representations⁸⁰. Optokinetic stimulation seeks to reduce spatial bias by repeatedly inducing reflexive orienting toward the contralesional hemispace through moving visual stimuli^{80,83}. More recently, non-invasive brain stimulation techniques, including repetitive transcranial magnetic stimulation and transcranial direct current stimulation, have been investigated to rebalance interhemispheric activity and improve attentional orienting⁸⁴. While these approaches have demonstrated promising effects in selected patient populations, evidence remains heterogeneous, and no single intervention has consistently shown superiority across individuals⁸⁵.

Overall, relearning approaches constitute one of the principal rehabilitation strategies for USN and aim to restore more balanced patterns of attentional allocation through repeated, task-specific, and structured practice⁸¹. Despite encouraging clinical results, their implementation is often limited by relatively low training intensity, limited adaptability to individual performance, and reduced patient engagement over prolonged rehabilitation⁸⁰. These limitations have stimulated growing interest in technology-assisted rehabilitation, particularly virtual reality and serious games, which provide controlled yet ecologically relevant environments capable of delivering intensive, standardized, and adaptive cognitive training^{86,87}. Moreover, recent extended reality systems are relatively straightforward to implement in clinical settings, requiring only limited setup while allowing therapists to administer standardized rehabilitation

Chapter 1 - General Introduction

protocols in a manner comparable to conventional computer-based interventions⁸⁶.

In this context, VR SG approaches may extend these paradigms by increasing engagement and training intensity, while enabling continuous adjustment of task difficulty based on individual performance^{88,89}. By embedding training within controlled interactive environments that incorporate feedback and reward mechanisms, these approaches may support sustained engagement and more effective practice conditions^{88,89,89}. Nevertheless, many existing implementations rely on fixed or manually adjusted task parameters, which may not adequately account for the heterogeneity of post-stroke cognitive and motor profiles or for fluctuations in performance over time⁹⁰. Dynamic Difficulty Adjustment (DDA) approaches represent a particularly promising direction⁹⁰. Rather than relying on fixed task parameters, SG implementing DDA systems can dynamically modulate task difficulty according to the participant's performance^{88,91}.

While elements of adaptivity and personalization for cognitive rehabilitation have been explored, their implementation remains fragmented, and their integration across multiple domains is limited⁹². One key challenge lies in the complexity of cognitive rehabilitation, where multiple functions are often impaired simultaneously and each function evolves differently over time, requiring continuous and multidimensional adaptation of task demands⁴⁴. More fundamentally, the implementation of effective DDA systems in this context requires not only real-time performance monitoring, but also sufficiently rigorous frameworks to guide the adaptation process and ensure that changes in task difficulty remain consistent, interpretable, and clinically meaningful⁹³. In this perspective, the development of more structured and principled adaptive approaches may represent a necessary step toward individualized and dynamically calibrated cognitive rehabilitation interventions.

Within this context, the REAsmash framework was developed to complement existing rehabilitation strategies rather than replace them. By

combining theory-driven task design, objective process-oriented assessment, and Dynamic Difficulty Adjustment, the framework enables the simultaneous evaluation and training of spatial attention and distractor inhibition while continuously adapting task demands according to individual performance. Moreover, the extended reality environment allows the continuous acquisition of objective behavioral markers, such as eye, head, and upper-limb movements, providing a richer characterization of patient performance than is typically achievable with conventional paper-and-pencil or standard computer-based rehabilitation approaches. In doing so, it addresses several limitations of conventional rehabilitation by promoting individualized training within a standardized experimental framework. Furthermore, the portability, relatively low cost, and limited infrastructure requirements of modern XR systems make them well suited for deployment beyond specialized rehabilitation centers, potentially expanding access to technology-assisted rehabilitation in resource-limited settings and geographically remote areas.

Objective of the present PhD thesis

This doctoral work was conducted within a broad research framework involving the integration of VR, SG, and adaptive training approaches for neurorehabilitation, encompassing the development of interactive assessment and rehabilitation systems^{92,94–100}. The present thesis builds upon the REAsmash SG paradigm, originally developed by our research team^{94–99} (presented in detail in Chapter 2). This thesis focuses on the methodological extensions of the REAsmash SG paradigm for assessment and adaptive modulation of neurorehabilitation following stroke.

The overarching objective of this thesis was to address limitations in the assessment and rehabilitation of post-stroke spatial attention and distractor inhibition deficits by extending an existing theory-driven VR SG paradigm into a broader assessment and rehabilitation framework, enabling more precise, quantitative, and adaptive investigation of cognitive processes. Four interrelated objectives were pursued.

Chapter 1 - General Introduction

The first objective was to extend the REAsmash paradigm to improve the characterization of attentional deficits by jointly assessing spatial attention and distractor inhibition within a unified framework. This objective was achieved throughout the thesis but started with the non-immersive VR version of the REAsmash task.

The second objective was to examine how the level of VR immersion influenced cognitive performance. By implementing and directly comparing non-immersive and immersive VR versions of the same paradigm, we investigated how interaction modality and environmental characteristics influenced spatial attention and distractor inhibition processes, providing implications for both assessment and deployment across a range of clinical contexts.

The third objective was to refine behavioral characterization through the integration of process-oriented measures. The development of the REAsmash-ET framework combined eye movement and upper limb kinematic recordings, enabling a detailed analysis of visual exploration and motor interaction responses, providing access to attentional dynamics that cannot be inferred from omission and response time outcome measures.

The fourth objective was to extend this assessment framework toward adaptive rehabilitation. A theory-driven DDA approach was developed to enable continuous and multidimensional adaptation of task demands based on individual performance and normative constraints. This framework allowed the simultaneous targeting of spatial attention and distractor inhibition within a personalized and scalable rehabilitation context.

Together, these objectives reflect progression from the extension of an existing experimental paradigm toward the development of integrated and adaptive tools for assessment and rehabilitation. By combining theoretical grounding, methodological innovation, and translational application, this thesis aimed to contribute to a more precise, dynamic, and functionally relevant approach to cognitive assessment and rehabilitation after stroke. While focused on the REAsmash paradigm and its associated assessment

framework, the results of the present thesis may be generalized to other SG frameworks.

Structure of the thesis

This thesis is manuscript-based. Each empirical chapter corresponds to an individual study that has been submitted to an international peer-review journal. Therefore, each chapter contributes to different aspects of the research developed throughout this thesis. Empirical Chapters 2, 3 and 4 have been published following peer-review. Chapter 5 is pre-print published and currently undergoing peer-review. The citations of the published and submitted papers are given at the beginning of each empirical chapter.

The first empirical chapter (Chapter 2) presents the first non-immersive implementation of the REAsmash paradigm and focuses on its use for assessing performance in a structured visual search task with post-stroke individuals. The study evaluates behavioral outcomes, including response time, errors, and omissions. It also introduces an additional spatial dimension by contrasting responses to targets presented in congruent and incongruent hemifields relative to the response hand in post-stroke and healthy participants. The aim was to improve the characterization of attentional deficits by jointly assessing spatial attention and distractor inhibition processes.

The second empirical chapter (Chapter 3) examines the influence of the level of VR immersion by directly comparing immersive and non-immersive versions of the same task paradigm. The study evaluates the transfer and comparability of performance measures across different implementations, with implications for both assessment and deployment across a range of clinical contexts.

The third empirical chapter (Chapter 4) introduces the REAsmash-ET framework as a methodological study integrating ET and upper limb kinematics within an immersive VR search-and-reach task. This research proposes an analytical approach adapted to the investigation of visual exploration and manual responses in peripersonal space, specifically for 3D

Chapter 1 - General Introduction

stimuli distributed across a horizontal interaction plane, thereby providing indirect access to attentional dynamics that cannot be captured by response time and omission outcome measures alone.

The final empirical chapter (Chapter 5) presents the development of a theory-driven DDA approach within the REAsmash framework. Building on the cross-platform evaluation and non-immersive implementation developed in previous chapters, the study introduces an adaptive algorithm that integrates individual performance with normative data to dynamically modulate spatial and non-spatial attention demand.

Together, these empirical chapters support an individualized approach to assessment and rehabilitation of attentional impairments after stroke. Overall, this thesis seeks to develop a better understanding of attentional impairments, and in parallel, develop clinically relevant tools that are better aligned with the challenges faced by stroke survivors in everyday life.

Chapter 2

A non-immersive virtual reality serious game to assess distractor inhibition and spatial target selection on response time attention in post-stroke individuals

Gregorio Sorrentino, Gauthier Everard, Florence Vanhoof, Thierry Lejeune and Martin Gareth Edwards

Published in

Smart Health, June 2025. DOI: 10.1016/j.smhl.2025.100595

Abstract

BACKGROUND: REAsmash, a non-immersive virtual reality serious game based on Feature Integration Theory (FIT) was used to evaluate distractor inhibition and spatial attention.

METHODS: Participants (15 post-stroke and 15 age matched healthy controls) performed the visual search REAsmash task with manipulations of high and low target-distractor salience and distractor number. Dependent variables included frequency of errors and omissions and mean correct response time.

RESULTS: Post-stroke participants made more errors ($\chi^2(1) = 19.452$, $p < 0.001$) and omissions ($\chi^2(1) = 55.108$, $p < 0.001$), and responded slower ($F(1,28) = 17.957$, $p < 0.001$, $\eta^2 = 0.391$) than controls. FIT significant effects showed salience ($F(1,28) = 497.626$, $p < 0.001$, $\eta^2 = 0.947$), distractor number ($F(2,56) = 24.968$, $p < 0.001$, $\eta^2 = 0.471$), and a salience and distractor number interaction ($F(2,56) = 26.616$, $p < 0.001$, $\eta^2 = 0.487$), with increased distractor number slowing response time in the low salience condition. A salience-by-group interaction ($F(1,28) = 7.794$, $p = 0.009$, $\eta^2 =$

Chapter 2

0.218) indicated greater post-stroke difficulties in low salience conditions. A target-hand congruency (Simon) effect was observed only in post-stroke participants ($F(1,28) = 4.499$, $p = 0.043$, $\eta^2 = 0.138$).

CONCLUSION: REAsmash-niVR replicated FIT results, confirming its validity for assessing distractor inhibition and spatial attention in post-stroke populations. Future research will compare individuals with and without visual neglect and explore rehabilitation applications to improve spatial attention and motor responses.

Keywords

Visual search; serious game; spatial attention; inhibition; executive functions; non immersive virtual reality.

Introduction

Stroke is the leading cause of long term disability in developed countries², with an estimated 80 million survivors worldwide living with disabilities¹⁰¹, and with expectations for a 35% increase in stroke prevalence between 2020 and 2030^{3,4}. Motor limitations are the most common post-stroke impairments, with an estimated prevalence of 83-90% in acute / sub-acute stages^{102–104}. Cognitive impairments resulting from stroke are less obvious, with prevalence in the acute / sub-acute stages estimates varying from 24 to 80%⁴⁴. Stroke survivors are often faced with enduring difficulties following clinical interventions in one or more cognitive functions, including attention, concentration, spatial awareness, inhibition, perception, memory, praxis, and executive functioning^{105–109}. Several factors contribute to this variability in prevalence estimation, including the heterogeneity of post stroke cognitive deficits, with clinical scenarios that can range from clear deficits of a specific cognition to, more commonly, conditions where several cognitive functions are involved^{13,110}. Furthermore, it is common to consider the motor impairments as independent to the cognitive impairments, presenting a limitation in understanding.

Executive functions, such as selective attention and cognitive inhibition are deeply involved in motor relearning processes^{111–114} and seem to have a direct association to poor motor performance^{115–117}. Furthermore, ecological (real-world) motor interaction tasks integrate cognitive load and double-task demands, requiring cognitive inhibition in order to perform the task efficiently^{18,118,119}. Even though the literature clearly shows the impact of cognition on post-stroke recovery^{18,120}, the routine assessment of cognitive deficits remains underrepresented in the clinic^{47,48}, unless the patient shows clearly observable cognitive impairments.

Differences in spatial task performance among post-stroke individuals may also reflect altered motor planning or execution, particularly when reaching across the midline¹²¹. The effect may be explained by the Simon effect¹²². The Simon effect refers to the phenomenon whereby reaction times are faster, and responses more accurate, when the spatial location of a stimulus

Chapter 2

corresponds to the side of the response hand, even if stimulus location is irrelevant to the task. This effect is thought to arise from automatic spatial coding of stimuli and subsequent response conflict and has been used as an index of executive function and motor planning¹²³. From a motor perspective, the effect may be linked to a requirement of greater postural control or coordination of the trunk and upper limb (i.e., driven by motor plan complexity). In this context, stimulus-response hand congruency may offer additional insight into the interplay between spatial and inhibitory attention.

Based on recent calls to improve neuropsychological evaluations using new technologies, our team recently developed REAsmash-iVR¹²⁴, a new immersive Virtual Reality (iVR) Serious Game (SG) with the aim to simultaneously evaluate distractor inhibition and spatial attention using measures of target omissions and response time during an immersive virtual experience (head-mounted display). The REAsmash-iVR is an adaptation of the classic fairground and arcade game Whac-A-Mole, and based on Feature Integration Theory (FIT)¹²⁵. FIT, by Treisman and Gelade, contrasted response time performance to two target-distractor contrast conditions. In a high saliency target-distractors contrast condition, the target differed by one salient feature from the distractors (e.g., a red target presented with blue distractors), leading to “parallel search” where the target “pops-out” from the distractors. This pre-attentive cognitive effect shows that attention is directly drawn to the target stimulus. In contrast, in a low saliency target-distractors condition, the target differs from the distractors by a conjunction of features (e.g., a red circular target presented with blue circular and red square distractors, with red and circle features of the target shared with the distractors). This stimuli condition leads to “serial search” where the participant spatially scans the stimuli one at a time, attentionally inhibiting the distractor stimuli until they find the target. Treisman and Gelade showed that in parallel search, increasing the numbers of distractors did not change response time¹²⁵. However, the serial search condition was influenced by distractor number, with increased numbers of distractors increasing response time. The REAsmash-iVR replicates the FIT paradigm using animated complex 3D stimuli¹²⁴.

The novelty of the REAsmash lies in applying the well-established FIT attentional principles within a SG format for the concurrent assessment of spatial attention (contrasting time to select a left versus right targets, a common test paradigm for neglect) and distractor inhibition. This integration allows for the identification of co-occurring (spatial and inhibitory) attentional deficits. The aim of this novel combination is to enable patient stratification based on attentional profiles, identifying individuals with hemiparesis with or without distractor inhibition difficulties, individuals with hemiparesis with or without lateralised spatial deficits, and individuals with hemiparesis and lateralised spatial deficits (neglect) with or without distractor inhibition difficulties. This novelty in diagnosis test allows a better understanding of patient profiles and may lead to predictions in the efficacy of treatment success (i.e., with profiles of attention impairments predicting compromising efficacy).

Previous research on cognitive assessment in aged participants has demonstrated better response to non-immersive VR (niVR) relative to iVR with the iVR sometimes causing participant stress¹²⁶. Stress can be further increased by the shorter proximity to stroke onset (i.e., time since stroke)¹²⁶. Nevertheless, recent studies involving immersive VR in older adults with cognitive decline have reported high levels of acceptance¹²⁷. This may be related to advancements in head-mounted displays, which reduce cyber sickness and provide immersive experiences that closely mimic real-world environments, reducing stress and anxiety¹²⁷. Therefore, the debate in the literature remains active, with findings highlighting both challenging and promising outcomes.

We decided to recreate the REAsmash in a non-immersive environment (i.e., REAsmash-niVR). Non-immersive VR is typically defined as interaction with digital content through input peripherals (e.g., keyboard, touchscreen or hand tracker) and an output device (e.g., screen or tablet)⁵⁷. The REAsmash-niVR adheres to this format by offering an interactive virtual environment on a large touch-sensitive screen (i.e., the REAtouch®), without the use of immersive head-mounted displays. This technology brings the advantages of VR, without increasing stress to individuals,

Chapter 2

thereby providing test quality suitable for acute and sub-acute patients^{128,129}. REAsmash can be used as an assessment tool in both clinical and research settings for cognitive impairments, supporting both diagnosis and future stratification of post-stroke patients thanks to its accessibility and user-friendly interface for both patients and clinicians.

Given the increasing clinical integration of VR technologies in neurorehabilitation, demonstrating standard cognitive effects in VR environments represents an essential step toward supporting their use in evidence-based assessment. In this context, we describe the technical implementation of the REAsmash-niVR and present a proof-of-concept investigation aimed at demonstrating its feasibility and sensitivity in detecting group-level attentional deficits. While the establishment of criterion validity against traditional neuropsychological measures remains a critical objective, it falls beyond the scope of this initial study.

We contrasted a group of 15 post-stroke participants with a control group of 15 mean age-matched healthy volunteers. Based on previous literature, we hypothesised an overall general FIT effect for all participants: (i) longer mean response time to accomplish the task in low compared to high salience conditions; and (ii) an interaction effect, with no effect of distractor number for the high salience condition and increased time to find the target with increased distractors in the low salience condition. Furthermore, we predicted (iii) an interaction between group and salience, with post-stroke participants exhibiting a specific difficulty in inhibiting distractors, characterised by slower responses, in the low salience condition, but with no significant group differences in the high salience condition.

In addition to the FIT effect and group differences, the REAsmash measures peripersonal space reaching responses, offering the possibility to investigate differences in the position of the target stimulus relative to the response hand.

In this study we contrasted target position relative to response hand (congruent vs incongruent hemi-field), making (iv) the hypothesis of a

target-response hand congruency effect showing faster responses for congruent relative to incongruent (i.e., showing a Simon effect¹²²), and no interactions with distractor salience, distractor number and group.

Materials and Methods

Study design

The protocol was approved by the Saint Luc-UCLouvain Hospital-Faculty Ethics Committee (Belgium) (2015/10FEV/053) and registered on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04694833) (NCT04694833).

Participants

Sample size estimation was guided by a power analysis performed using G*Power® (version 3.1.9.7), and data from a previous study that investigated the REAsmash interaction between target-distractor saliency and distractor number (FIT)¹²⁴. This interaction effect underlies the task objective to measure distractor inhibition. From these data (healthy participants) a significant interaction effect was reported ($F(2,114) = 117.58$, $p < 0.001$, $\eta^2 = 0.67$), with an associated effect size (Cohen's f) of 1.425. Based on these parameters, the power analysis indicated that a sample of 4 participants would be sufficient to detect this interaction with 80% power at an alpha level of 0.05. Since our study involved a between-group design comparing post-stroke participants with healthy controls, we opted for a more conservative sample size of 15 participants per group. A post-hoc power check confirmed this sample was sufficient to detect the observed between-group effect ($\eta^2 = 0.391$).

Post-stroke participants were recruited from the physical medicine and rehabilitation department of the Cliniques universitaires Saint-Luc in Brussels, and all were hospitalised or discharged patients. The inclusion criteria were: (1) presence of an ischemic or haemorrhagic first cortical and/or sub-cortical stroke, diagnosed by CT (computed tomography) or MRI (magnetic resonance imaging) and (2) a good understanding of the task instructions. The latter was assessed through a verbal walkthrough of the

Chapter 2

task with verbal confirmation followed by a simulated brief trial practice session. Participants were included only if they successfully completed the practice. The exclusion criteria were: (1) uncorrected vision deficiencies (e.g., hemianopia, peripheral vision loss, amblyopia, color blindness or uncorrectable visual acuity deficits); (2) the presence of other neurological conditions (e.g., dementia or extrapyramidal disorders) or orthopaedic dysfunction that could influence upper extremity function; (3) cognitive impairment (indicated either by MoCA scores⁴⁶ below 20 out of 30, administered no more than 7 days prior to the trial, or by an inability to complete the practice task) and (4) too poor trunk control to sustain the trial. Recruitment started in February 2023 and ended in June 2024. The post-stroke participants group consisted of 15 participants (1 female, all right-handed) with an average age of 59.6 years ($SD = 13.0$), 1 non-naïve for VR. Average time from the stroke was of 13 months ($SD = 13$) with 9 participants in sub-acute phase and 6 in chronic phase at the time of the trial, average MoCA score was of 26.2 ($SD = 2$) (See Table 1).

From the 15 participants, 8 had a history of visual spatial attention deficits reported in the medical records. We therefore tested all post-stroke participants with gold standard tests for spatial attention at the time of testing. Further, we conducted a post-hoc analysis (first post-hoc analysis) on participants without signs of visual USN at the time of testing relative to healthy controls. The post-hoc sample was composed of 12 participants (1 female, all right-handed, average age 59.5 years, $SD = 14.3$). See the Procedure section for details of the gold standard tests.

Table1. The demographic characteristics of the post-stroke participants.

ID	Sex	Age (years)	Height (cm)	VR naive	The response hand was the dominant one?	Months from the stroke	Stroke type	Brain lesion side	Brain lesion location	MoCA score	History of spatial attention impairment	Current spatial attention impairment	Current Rehabilitation
P1	M	69	172	Yes	Yes	6	Hem	Right	Sylv+Deep	26	Yes	No	Nps+OT+PT
P2	M	65	176	Yes	No	2	Isch	Left	MCA	25	No	No	Nps+OT+PT
P3	M	62	183	Yes	Yes	5	Isch	Right	MCA	27	Yes	Yes	Nps+OT+PT
P4	M	53	173	Yes	No	4	Isch+Hem	Left	Sylv	20	No	No	Nps
P5	M	65	180	Yes	No	38	Isch	Left	MCA	26	No	No	No more
P6	F	52	166	Yes	No	20	Isch	Left	Sylv	26	No	No	PT
P7	M	52	178	Yes	Yes	23	Isch	Right	Sylv	28	Yes	Yes	No more
P8	M	62	164	Yes	No	16	Hem	Left	MCA	25	No	No	No more
P9	M	64	181	Yes	Yes	41	Isch	Right	Sylv	27	No	No	PT
P10	M	54	180	Yes	Yes	23	Isch+Hem	Right	Sylv	28	Yes	No	No more
P11	M	21	172	No	Yes	2	Hem	Right	Sylv	26	Yes	No	Nps+OT+PT
P12	M	60	182	Yes	Yes	3	Isch	Right	Sylv	26	Yes	No	Nps+OT+PT
P13	M	71	173	Yes	No	5	Isch	Left	MCA	28	No	No	Phys
P14	M	66	178	Yes	Yes	4	Isch	Right	MCA	28	Yes	Yes	Nps+OT+PT
P15	M	78	178	Yes	Yes	4	Isch	Right	Sylv	27	Yes	No	Nps+OT+PT

F = Female, M = Male; Isch= Ischemic, Hem= Hemorrhagic; MCA= Middle cerebral artery, Sylv= Sylvian Segment of MCA; Nps= neuropsychological therapy, OT= Occupational Therapy, PT = Physiotherapy.

Chapter 2

The group of 15 healthy adults (7 females, 4 left-handed), with an average age of 57.9 years (SD = 14.0), were recruited between November 2021 and March 2024 through the University of Louvain participation panel and social media groups (See Table 2). The participants had normal or corrected to normal vision and no neurological, psychiatric or orthopaedic disorders potentially affecting compliance or limiting cognition and / or upper limb functionality. Difficulty in understanding French (the language of the task instructions) was an exclusion criterion. Two healthy volunteers were non-naïve for VR.

	Sex	Age	Height (cm)	VR naïve	Dominant hand
HS1	M	48	180	No	Right
HS2	F	21	168	Yes	Right
HS3	M	45	178	Yes	Left
HS4	F	54	166	Yes	Left
HS5	F	67	174	Yes	Right
HS6	M	55	182	Yes	Right
HS7	M	61	181	Yes	Left
HS8	M	75	178	Yes	Left
HS9	M	65	173	Yes	Right
HS10	F	55	164	Yes	Right
HS11	M	61	180	Yes	Right
HS12	F	64	165	Yes	Right
HS13	F	64	163	Yes	Right
HS14	F	81	164	Yes	Right
HS15	M	52	184	No	Right

Table2. The demographic characteristics of the healthy participants.

F = Female; M = Male.

The post-stroke and control groups were mean age matched (59.6 years vs 57.9 years respectively, with a t-test showing no significant difference in

age between the two groups ($t(28) = 0.351, p = 0.726$). All the participants volunteered to participate in the study, providing written informed consent before participation.

Materials

The REAsmash-niVR was developed to run on the REAtouch® (Axinesis®) interactive medical device. This was composed of a touch-sensitive screen (43", 95 x 53 cm) incorporated in a motorised structure that allowed customised screen lifting and inclination tilting (Fig. 1). The REAtouch® provides multisensory and real-time performance feedback and is designed to allow uni- or bi-manual interaction by direct hand-contact with the screen.



Figure 1. The non-immersiveVR device. REAtouch® (Axinesis®) touch-sensitive 43" screen tablet with multisensory and real-time performance feedback. The height and inclination of the screen can be adjusted. In the present study, the inclination was the same as that presented here (i.e., 0°).

Chapter 2

The REAsmash was developed using Unity 2019.3 software (C#). It displayed a cartoon-like garden containing 24 molehills (6 columns and 4 rows), placed on an active playing surface of 95x42cm. The stimuli consisted of moles emerging from the molehills, with each mole and molehill covering a surface of 8x8cm. The stimuli were presented in 7 trial blocks, with the target mole (wearing a red miner's helmet) pseudo-randomly appearing one time from each of the 24 molehills for each trial block, making 24 trials. In the baseline (level 1), no distractors were presented with the target mole, allowing a baseline measure of participants response time without distractor inhibition demands. In the high saliency target-distractor contrast conditions, the target was presented with distractor moles wearing blue helmets (miner's or horned) (levels 2, 3 and 4). In the low saliency target-distractor contrast conditions, the target was presented with distractor moles wearing blue miner's or red horned helmets (levels 5, 6 and 7), with the distractors sharing a conjunction of features with the target. In each of the two target-distractor salience conditions, 11, 17 or 23 distractors accompanied the target (respectively), making randomised stimuli sets of 12, 18 and 24 stimuli (Fig. 2).

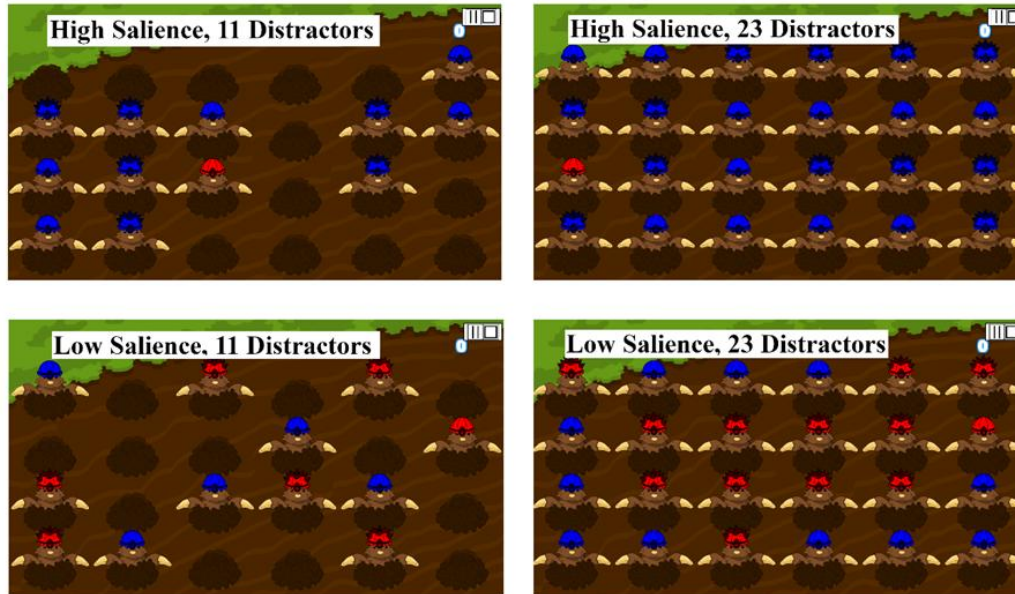


Figure 2. Target-distractor search stimuli. Examples of stimulus settings in: (i) Levels 2 and 4 (i.e., high saliency) with 11 and 23 distractors wearing horned or miner's blue helmets and (ii) levels 5 and 7 (i.e., low saliency) with 11 and 23 distractors wearing red helmets with horns or blue miner's helmets. For both high and low saliency conditions, there were two intermediate levels (i.e. levels 3 and 6) with 17 distractors.

Procedure

The study was run in a controlled laboratory at the Cliniques universitaires Saint-Luc of Brussels (Belgium). Participants were asked to sit on a chair, with their feet on the ground, positioned in front of the REAtouch[®] and aligned with the central sagittal axis of the interactive touch-sensitive screen. For participants in wheelchairs, the wheelchair was appropriately positioned to align the participant in the same playing conditions as the other participants, with their feet placed on the footrest of the wheelchair. The screen was adjusted to a suitable height to make the reaching span of the participant comfortable and safe. The touch-sensitive screen was presented at a horizontal angle of zero degrees relative to the ground. The

Chapter 2

participants were instructed to begin each trial by touching a “X” with their playing hand that appeared in the central mid-lower edge of the touchscreen. This was used to provide a consistent starting point prior to each trial response. After touching the start position, the trial began, and the participant was instructed to touch the target as quickly as possible using their dominant hand in the case of healthy control participants and the less-impaired hand in the case of post-stroke participants. This approach helped to minimise the impact of motor impairments, ensuring a clearer assessment of cognitive function. The instructions were given orally by the examiner before the start of the session and displayed on the touchscreen immediately before the session began. Prior to the main experiment, a 10-trial practice session was used to familiarise participants with the test and device. A 20-second rest period was provided between each of the 7 trial blocks (24 trials in each block; 168 total trials). The trial blocks were run from easy to difficult levels (1-7). Each target stimulus was presented for a maximum duration of 7 seconds. Correctly responding to the target within 7 seconds was designated as a correct response time (i.e., the time between the beginning of the stimuli presentation and the manual response). Omissions were defined as the target not being found within the 7 seconds, and errors responses were defined by the participant responding to a distractor instead of the target. For all manual response (irrespective of correct or incorrect), the position of final response on the stimulus playing field was recorded, along with the position of the target stimulus for that trial. Participants, including those with cognitive deficits, completed the full assessment in under 10 minutes (average time approximately 8 minutes).

All post-stroke participants underwent a battery of neuropsychological tests to explore spatial attention within 7 days of the niVR session. This assessment included the Bells Test³⁰, a paper-and-pencil cancellation task in which participants are asked to circle bell figures scattered among various distractor figures. This test evaluates egocentric neglect by examining the number and spatial distribution of target omissions across the visual field. In addition, participants completed the Apple Cancellation Test¹³⁰, which is specifically designed to distinguish between egocentric and allocentric neglect. In this task, participants must identify and cancel only complete

apple figures while ignoring distractor apples that are incomplete on either the left or right side. As for the Bells Test, egocentric neglect is defined by a difference in target omissions for contralesional relative to ipsilesional targets. Allocentric neglect is defined by error responses to the incomplete distractors, and more errors when the incomplete side is contralesional relative to ipsilesional. Finally, participants were assessed using the Visual Field and Visual Scanning subtests from the computerised Test for Attentional Performance (TAP) battery¹³¹. The Visual Field subtest assesses the presence of visual field deficits by measuring detection speed across various spatial locations, while the Visual Scanning subtest evaluates the participant's ability to systematically explore and search for targets within a structured visual array. Participants were considered to have visual USN if they had pathological results in any of the tests. Results showed that participants either showed peri-personal egocentric USN on all tests or showed no evidence of USN. There are no validated gold standard tests that systematically assess distractor inhibition impairments when searching for a target.

Data analyses

Data analyses were performed using SPSS 27.0 (IBM®). Omissions and error percentage responses were analysed using chi-square analysis (relative to correct responses). Mean correct response time analyses were first verified for data normality using the Shapiro-Wilk test, and then analyses were made using repeated measures ANOVAs. Post-hoc analyses were performed with Bonferroni with corrections for multiple comparisons.

The independent within-participant variables were target-distractor saliency (high vs low), distractor number (11, 17 and 23), and target-response hand congruency (congruent vs incongruent). For example, when participants played with their right hand, targets presented in columns 1-3 (i.e., left hemifield) were defined as incongruent targets, and targets presented in columns 4-6 (i.e., right hemifield) were defined as congruent targets. This definition was used to align the Simon effect relative to spatial targets, whereby incongruent trial corresponds to targets positioned in contralesional

Chapter 2

space. For the within-participant manipulations (2x3x2; 144 trials across 6 levels), a mean derived from 12 trials (collapsing target position) were used. We also tested the between-participants variable of group (post-stroke vs healthy). The dependant variables were omissions, error responses and correct target response time. Mean response time refers to the time between the appearance of the target mole stimulus and the response to correctly touch the target. Mixed measures ANOVA were used to test within-participant variability across task conditions (i.e., salience, distractor number, and target-hand congruency), and between participant groups.

Results

All participants completed the experiment without adverse event. In a general feedback discussion session with the participants after the study, they all described the experimental tasks as non-stressful and engaging. No participants asked to stop the experiment prematurely or to extend the rest periods.

For the post-stroke participant group, from the total dataset of 2520 trials (i.e., 7 levels x 24 trials x 15 participants), 51 trials were excluded due to technical issues in data collection. From the remaining 2469 trials, there were 76 omissions (3.1%), 37 error responses (1.5%) and 0 anticipatory responses (i.e., responses executed in less than 250ms). For healthy controls, from the total dataset of 2520 trials, there was one trial excluded due to technical issues. From the remaining 2519 trials, there were 9 omissions (0.3%), 8 error responses (0.4%) and 1 anticipatory response (0.04%). We used a standard practice three standard deviation confidence interval filter for response time to remove 36 outliers (1.4%) from the control data. No outlier filter was applied to the patient data.

Chi-square analyses for error and omission rates relative to correct responses, showed a significant group effect. The post-stroke participants committed significantly more errors and omissions than healthy participants ($X^2(1) = 19.452$, $p < 0.001$ and $X^2(1) = 55.108$, $p < 0.001$ for errors and omissions respectively, on a dataset of $N = 4988$). Because of the low

number of omissions and error responses, no further analyses could be conducted.

The ANOVA for mean response time showed a significant between-participants group effect, ($F(1,28) = 17.957, p < 0.001, \eta^2 = 0.391$), with slower mean response times for the post-stroke relative to healthy participant group (mean 1571ms, SD 69.905 and 1152ms, SD 69.905 for post-stroke and healthy participants respectively). The ANOVA supported the FIT effect, showing within-participants main effects of saliency, ($F(1,28) = 497.626, p < 0.001, \eta^2 = 0.947$) and number of distractors ($F(2,56) = 24.968, p < 0.001, \eta^2 = 0.471$). As predicted, the results showed faster responses in high (mean 900ms, SD 45.531) compared to low (mean 1824, SD 60.584) target-distractor salience conditions and increased response time with increased numbers of distractors (mean 1276ms, SD 52.310; mean 1371ms, SD 52.726 and mean 1439ms, SD 48.533 for 11, 17 and 23 distractors respectively) (Fig. 3.a). There was also a significant main effect of target-hand congruency ($F(1,28) = 10.414, p = 0.003, \eta^2 = 0.271$), with slower mean response times when target position was incongruent to the response hand (mean 1440ms, SD 65.249) compared to congruent (mean 1284ms, SD 42.279). Significant interactions were found between saliency and number of distractors ($F(2,56) = 26.616, p < 0.001, \eta^2 = 0.487$) (replicating the FIT effect) and between saliency and group ($F(1,28) = 7.794, p = 0.009, \eta^2 = 0.218$) (Fig. 3). Target-hand congruency and group was also significant ($F(1,28) = 4.499, p = 0.043, \eta^2 = 0.138$). No other interactions were significant.

To analyse the interactions, separate ANOVAs were run for each saliency condition and group. Concerning the interactions with the saliency condition, the high saliency target-distractor condition showed no significant differences for number of distractors or group. However, for the low saliency target-distractor condition, there was a significant effect for distractor number ($F(2,56) = 30.005, p < 0.001, \eta^2 = 0.517$) (as predicted by the FIT effect) and group ($F(1,28) = 19.459, p < 0.001, \eta^2 = 0.970$). Analysis of distractor number showed increased mean response time increased with increased numbers of distractors (mean 1656ms, SD 65.587;

Chapter 2

mean 1831ms, SD 67.865 and mean 1984ms, SD 62.464 with 11, 17 and 23 distractors respectively). Analysis of group showed slower mean response times for the post-stroke relative to healthy participant group (mean 2091ms, SD 85.678 and mean 1556ms, SD 85.678 respectively).

Concerning target-hand congruency interaction with group, healthy participants showed no target-hand congruency effect ($F(1,14) = 1.754$, $p = 0.207$, $\eta^2 = 0.111$). However, post-stroke participants showed a significant main target-hand congruency effect ($F(1,28) = 8.661$, $p = 0.011$, $\eta^2 = 0.382$) with mean response times slower for incongruent (mean 1700ms, SD 122.849) relative congruent (mean 1443ms, SD 68.548) condition (Fig. 3.b).

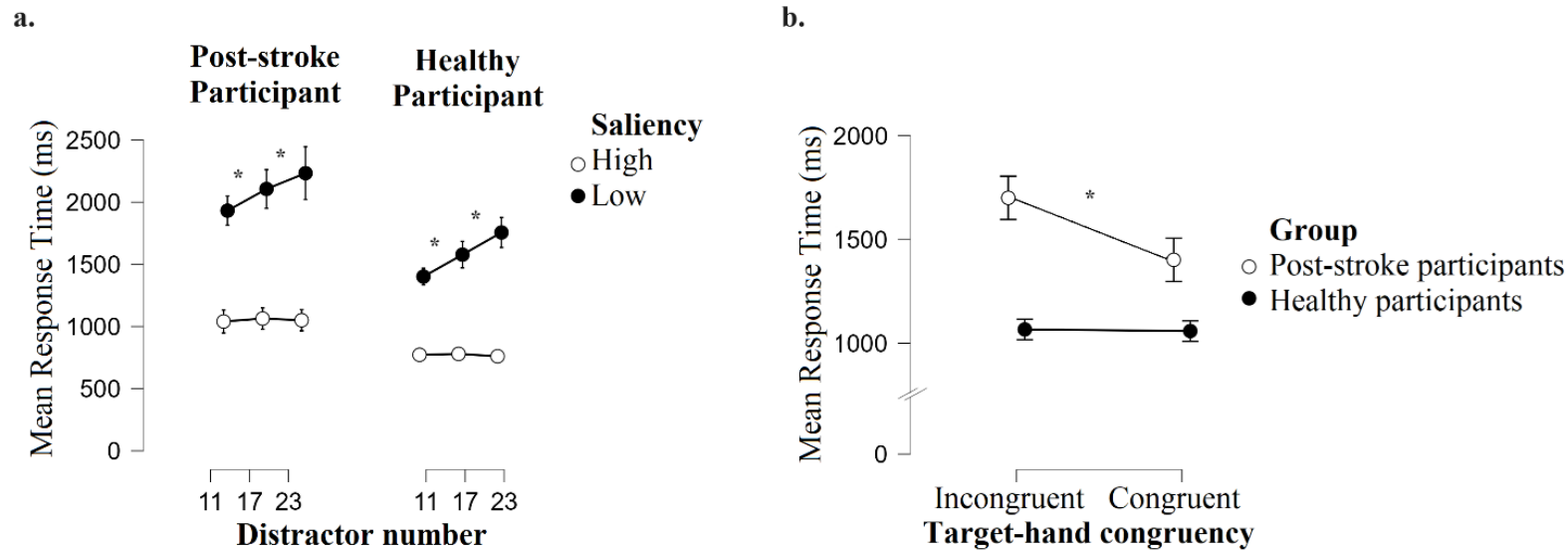


Figure 3.a Number of distractors and target-distractor saliency interaction for mean response. Presentation of the mean response time (in milliseconds) as a function of distractor number and target-distractor saliency contrast. On the Y-axis the response time. On the X-axis the three possible distractor number conditions (11, 17 and 23). Outlined circles represent high salience conditions; black-filled circles represent low salience conditions. On the left, the group of post-stroke participants and on the right, the healthy controls. The error bars show the 95% confidence interval. “*” represent significant main effect for distractor number.

Figure 3.b. Mean response times levels from 2 to 7 organised according to target-hand congruency, in post-stroke with sequelae vs healthy controls groups. Presentation of the mean response times (in milliseconds) in

Chapter 2

successful trials with target emerging in the two alternative positions. On the Y-axis the mean response time. On the X-axis the two possible target position (i.e., hemifield contralateral vs. ipsilateral to the playing hand). The error bars show the 95% confidence interval. Outlined circles represent post-stroke participants; black-filled circles represent healthy controls. “” represent significant main effect of target-hand congruency.*

For the first post-hoc analysis, we removed three participants diagnosed with visual USN within 7 days prior to niVR session. The objective of this analysis was to test if the significant interactions between saliency and group, and target-hand congruency and group mean response time was caused by the inclusion of these three participants with spatial attention impairments. The ANOVA of the mean response times confirmed the same significant effects. There was a significant effect of group ($F(1,25) = 12.695$, $p = 0.002$, $\eta^2 = 0.337$), target-distractor saliency ($F(1,25) = 559.773$, $p < 0.001$, $\eta^2 = 0.957$) and distractor number ($F(1,25) = 27.365$, $p < 0.001$, $\eta^2 = 0.523$). Significant interactions were found between saliency and group ($F(1,25) = 13.478$, $p = 0.001$, $\eta^2 = 0.350$) and saliency and distractor number ($F(2,50) = 27.097$, $p < 0.001$, $\eta^2 = 0.520$). Target-hand congruency also remained significant ($F(1,25) = 6.780$, $p = 0.015$, $\eta^2 = 0.213$), but now with no interaction between target-hand congruency and group ($F(1,25) = 2.363$, $p = 0.137$, $\eta^2 = 0.086$).

The second post-hoc analysis focused on the baseline level, contrasting the 15 post-stroke participants with the 15 healthy controls. The aim of this analysis was to explore the effect of target position (congruent vs incongruent hemi-field) relative to the response hand on mean response time in a search task without distractor inhibition demands. The ANOVA on mean response times showed a main target-hand congruency effect ($F(1,28) = 8.982$, $p = 0.006$, $\eta^2 = 0.243$) and a significant interaction between target-hand congruency and group ($F(1,28) = 7.801$, $p = 0.009$, $\eta^2 = 0.218$). Separate ANOVAs per group showed a target-hand congruency effect only in the post-stroke participants group ($F(1,14) = 10.271$, $p = 0.006$, $\eta^2 = 0.423$), with longer response times in the incongruent target-hand condition (mean 1026.593ms, SD 126.509 and mean 801.288ms, SD 76.463 respectively) (Fig. 4).

Chapter 2

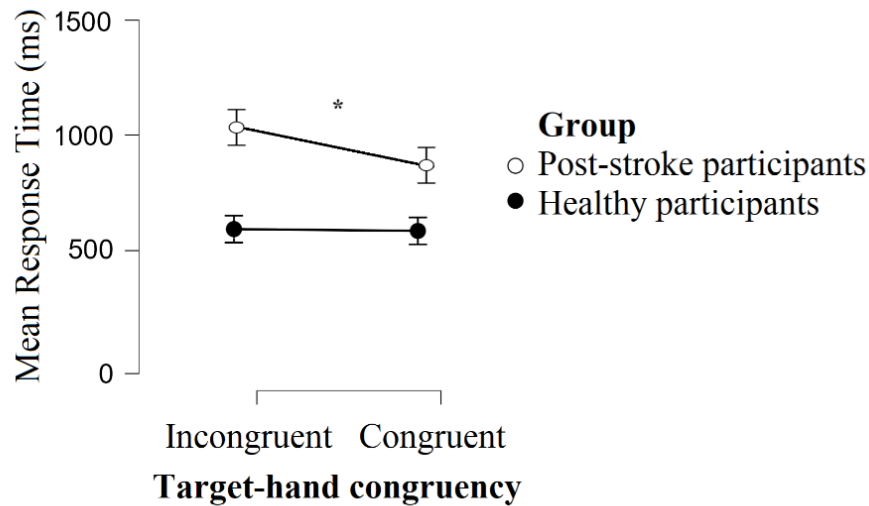


Figure 4. Mean response times in baseline level organised according to target-hand congruency, in post-stroke with sequelae vs healthy controls groups. Presentation of the mean response times (in milliseconds) in successful trials of level 1 with target emerging in the two alternative positions. On the Y-axis the mean response time. On the X-axis the two possible target position (i.e., hemifield contralateral vs. ipsilateral to the playing hand). The error bars show the 95% confidence interval. Outlined circles represent post-stroke participants; black-filled circles represent healthy controls. “*” represent significant main effect of target-hand congruency.

Combining the two planned post-hoc analyses, a further ANOVA contrasting the healthy controls with the 12 post-stroke participants without signs of visual USN showed a main target-hand congruency effect ($F(1,25) = 6.904$, $p = 0.014$, $\eta^2 = 0.216$) and a significant interaction between group and target-hand congruency ($F(1,25) = 5.052$, $p = 0.034$, $\eta^2 = 0.168$). Separate ANOVAs per group showed a target-hand congruency effect only in the post-stroke participants group ($F(1,11) = 24.043$, $p < 0.001$, $\eta^2 = 0.686$).

Discussion

Compared to currently available gold standard diagnosis tests, the REAsmash SG, based on Feature Integration Theory (FIT)¹²⁵, provides a novel systematic evaluation of distractor inhibition attention. Further, the REAsmash SG involves direct reaching responses to the target stimuli in peripersonal space, providing interesting target-hand congruency response time measures that depend on the spatial position of the target relative to the response hand.

This present study aimed to provide a preliminary investigation into the potential of the niVR version of REAsmash as a diagnostic tool for distractor inhibition. We contrasted, for the first time, the mean response times of post-stroke participants and healthy controls. Our results replicated Ajana et al.²⁹ who presented the iVR version of REAsmash SG on healthy aged adults, further demonstrating a replication of the FIT effect using gamified stimuli. Post-stroke participant outcomes probed the presence of specific attentional and motor response selection deficits that might remain undetected by conventional clinical assessments. The observed group differences, including the Simon effects, underscore the value of a task sensitive to both spatial and non-spatial aspects of attention.

The analyses of mean response time supported the FIT effect, characterised by longer mean response times to find and point to the target in low compared to high salience conditions (hypothesis 1), and an interaction effect (hypothesis 2), with no effect of distractor number for the high salience condition, but increased time to find the target with increased distractor numbers in the low salience condition.

For mean response time, we also reported a main effect of group, with the post-stroke group responding slower than the healthy control group. The third hypothesis predicted an interaction between saliency and group, which was supported. In the high salience condition with low distractor inhibition demands, there were no differences in mean response times. However, for the low salience condition with high distractor inhibition demands, the post-

Chapter 2

stroke participants were significantly slower than the control group. This finding suggests potential inhibition difficulties in the post-stroke participants. This interaction remained consistent in the first post-hoc analysis, where participants with visual USN were excluded, suggesting that the effect was not simply driven by the presence of USN in some individuals.

The fourth hypothesis, which predicted a target-hand congruency (Simon effect) effect, was confirmed in the principal analyses. Mean response time analyses showed an interaction between target-hand congruency and group, demonstrating significant differences in mean response times only for the post stroke group. Interestingly, we found this same effect in the baseline post-hoc analysis. In the present version of the REAsmash SG, we introduced a baseline level (level 1), making it possible to benchmark response times to targets presented without distractor inhibition demands. As for the principal analysis of data, this analysis of baseline demonstrated a significant interaction between target-hand congruency and group, with a target-hand congruency effect only in the post-stroke participants group, and longer response times in the incongruent than congruent target-hand condition. This suggests that the interaction effect is unrelated to distractor inhibition cognition, and more related to hand response after target attention selection. The interaction between target-hand congruency and group disappeared in the post-hoc ANOVA on the selected group of 12 post-stroke participants without signs of visual USN. However, the interaction between target-hand congruency and group for the baseline post-hoc ANOVA on the selected group of 12 post-stroke participants again showed the same interaction effect as the principal results. This variance in consistency of results would merit further investigation with a larger sample of participants with and without signs of spatial attention deficit in order to understand whether the target-hand congruency and group interaction is caused by spatial attention impairments.

The results of the present paper, and the paper by Ajana et al¹³² demonstrate that the REAsmash (iVR and niVR versions) provides a new assessment of distractor inhibition demands on spatial target search performance. The SG

was well received by participants, demonstrating the potential value that the test brings to testing participants, and maintaining their motivation. In line with the observed attentional patterns, we plan to conduct dedicated analyses on participants diagnosed with visual USN. Future investigations will explore the reliability of REAsmash in detecting spatial lateral biases (i.e., slower response times to contralesional versus ipsilesional targets) in individuals with USN. These analyses will help disentangle spatial attentional impairments from motor planning or execution difficulties. A preliminary version of these analyses, based on the participants identified with USN in the present data using gold-standard tests is provided as Supplementary Materials. Embedding both spatial target selection and distractor inhibition into a single SG framework offers a promising avenue for stratifying stroke survivors, for instance by differentiating patients with hemiparesis with or without co-occurring inhibitory deficits, distinguishing patients with hemiparesis with or without spatial attention impairments and distinguishing patients with hemiparesis and spatial attention impairments with or without co-occurring inhibitory deficits.

The target-hand congruency effect and group interaction results are interesting as they highlight a potential difference for post-stroke participants. The results suggests that this difference is not caused by distractor inhibition, but rather is more likely linked to problems in motor processes related to the cortical or subcortical lesion. Particularly when the task requires reaching movements across the midline, the increased demand for postural control and coordination of the trunk and upper limb may expose impairments in motor planning or execution in post-stroke individuals. It is well known that individuals post-stroke often face impairments in trunk control^{133,134}. The trunk plays a crucial role in stabilising the pelvis and supporting upper limb movements, enabling coordinated reaching tasks and maintaining overall core stability during functional activities¹³⁵. Furthermore, previous research has demonstrated that even the less-affected upper limb may exhibit subtle yet functionally relevant motor deficits in post-stroke individuals, particularly during reaching movements that require proximal arm control and precision^{136,137}. Although cognitive causes cannot be ruled out, such ipsilesional

Chapter 2

impairments can influence motor response strategies, contributing to prolonged response times and increased variability in movement trajectories, even in the absence of overt functional limitations in the post-stroke population. Lateral and diagonal reaching, especially to distant, such as those needed in the target-hand incongruent condition of our SG, required greater trunk control than the congruent condition¹³⁸. The incongruent target-hand condition could therefore constitute a further motor challenge for stroke survivors. Future studies on REAsmash could benefit from the introduction of a trunk control rating scale (as the Trunk Impairment Scale^{139,140}) in the assessment battery.

The present study has nevertheless some limitations. We chose not to divide participants based on their stage of post-stroke recovery, principally due to the participants sample size. However, the stage of recovery (subacute vs chronic) could impact outcomes in complex task such as REAsmash. Controlling for gender was not prioritised, as the FIT processes under investigation generally believed to operate independently of gender-related differences¹²⁵. Nevertheless, gender-based differences may provide meaningful insights into other factors, such as differences in engagement of the SG. Another limitation is that our sample included both participants with prior VR experience and VR naïve. Given the cross-sectional clinical design of this study, lack of familiarity with VR may have influenced the findings. Future research, aiming to establish REAsmash as a diagnostic tool, should explore how recovery phases, gender and familiarity with VR may influence outcomes in both iVR and niVR versions.

We plan to include 3 populations (i.e., (i) post-stroke participants with signs of visual USN on gold standard tests, (ii) post-stroke participants without signs of visual USN on gold standard tests and (iii) healthy controls). This will allow for further understanding of the interactions between distractor inhibition attention, spatial attention and target-response hand congruency effects post stroke. Furthermore, contrasting results between the REAsmash iVR and niVR versions on the same participants, we hypothesise that the two tests will show the same results (i.e., equivalence). These data will be important for developing tests to be used with post-stroke individuals in the

acute to sub-acute stages, starting with niVR, and transferring to iVR versions that can be used by post-stroke individuals in the sub-acute to chronic stages, particularly for outpatient diagnosis measures.

Beyond diagnostic potential, the REAsmash offers practical advantages in rehabilitation. The motivational affordances of serious gaming are known to enhance engagement and reduce performance variability across sessions, thereby enabling more consistent longitudinal tracking of patient progress⁶¹. We are currently conducting studies aimed at validating rehabilitation-oriented versions of REAsmash that specifically challenges difficulties experienced by the post-stroke individual (i.e., distractor inhibition attention vs spatial target-hand congruency and motor impairment). Future publications will report on their effectiveness, allowing clinicians and researchers to follow the evolution of this tool for neurorehabilitation purposes.

Conclusions

In conclusion, we have shown that REAsmash niVR test provides measures of non-spatial distractor inhibition attention, replicating the results of the iVR version, and the FIT paradigm. The REAsmash provides an ideal candidate to study whether and how distractor inhibition demand influences attention performance. Future studies will explore the effects of different degrees of immersion (iVR vs niVR) for the REAsmash and will contrast groups of participants with and without signs of visual USN to better understand distractor inhibition, spatial attention and target-response hand congruency effect in stroke survivors.

Funding

This work was supported by the Région Wallonne (SPW Economie-Emploi-Recherche) Win²Wal Program (convention no. SPE-Economie-Emploi-Recherche Win²Wal Program 1810108) and the Special Research Fund (FSR) of the French Community of Belgium, awarded by the University of Louvain.

Chapter 2

Availability of Data and Materials

The datasets used during the current study are openly available in the open data archive of University of Louvain (<https://dataverse.uclouvain.be/dataset.xhtml?persistentId=doi:10.14428/DVN/OM0TIM>).

Author Contributions

GS designed the presented study, collected and analysed the data, interpreted the results and wrote the paper. GE, TL, MGE created the REAsmash iVR, interpreted the results of the present paper and helped write the paper. FV interpreted the results of the present paper and helped write the paper. All authors contributed to editorial revisions in the manuscript. All authors read and approved the final manuscript. All authors have participated actively in the work and accepted responsibility for all aspects of the work.

Ethics Approval and Consent to Participate

All participants signed a written informed consent form according to the Helsinki Declaration. The Hospital Ethics Committee of the Cliniques universitaires Saint-Luc (Brussels, Belgium) authorised the current analysis procedure. The protocol identification number is NCT04694833.

Acknowledgment

We thank Julien Sapin (AXINESIS) for providing advice and technical support with the REAtouch[®] used in the project.

Conflict of Interest

The authors declare no conflicts of interest.

AXINESIS had no role in the design of the study, the data collection and analyses, the decision to publish, and in the preparation and writing of the manuscript.

Supplementary Material

Supplementary Analysis: Spatial Performance in Participants with Visual USN

This supplementary section reports exploratory analyses (requested by peer-review) for the participants diagnosed with USN. Mean response times of successful trials for participants with confirmed left visual USN ($N = 3$) were compared to those of the control group. Mixed measures ANOVAs were used to test within-participant variability across task conditions (i.e., saliency, distractor number, and target-hand congruency) and between participant groups.

Results and Discussion

The ANOVA for mean response time showed a significant between-participants group effect, ($F(1,16) = 34.748$, $p < 0.001$, $\eta^2 = 0.685$), with slower mean response times for the post-stroke with visual USN relative to healthy participant group (mean 1831ms, SD 105.116 and 1152ms, SD 47.009 for post-stroke and healthy participants respectively). The ANOVA showed within-participants main effects of saliency, ($F(1,16) = 225.046$, $p < 0.001$, $\eta^2 = 0.934$) and number of distractors ($F(2,32) = 4.481$, $p = 0.019$, $\eta^2 = 0.219$). There was also a significant main effect of target-hand congruency ($F(1,16) = 22.441$, $p < 0.001$, $\eta^2 = 0.584$), with slower mean response times when target position was incongruent to the response hand (mean 1620ms, SD 67.799) compared to congruent (mean 1363ms, SD 59.179). Significant interactions were found between saliency and number of distractors ($F(2,32) = 6.574$, $p = 0.004$, $\eta^2 = 0.291$) and between target-hand congruency and group ($F(1,16) = 14.102$, $p = 0.002$, $\eta^2 = 0.468$). No other interactions were significant.

To analyse the interactions, separate ANOVAs were run for each saliency condition and group.

Concerning the interactions with the saliency condition, the high saliency target-distractor condition showed no significant differences for number of

Chapter 2

distractors. The group effect was significant ($F(1,16) = 39.858, p < 0.001, \eta^2 = 0.714$).

For the low saliency target-distractor condition, there was a significant effect for distractor number ($F(2,32) = 6.341, p = 0.005, \eta^2 = 0.284$) and group ($F(1,16) = 21.990, p < 0.001, \eta^2 = 0.579$). Analysis of distractor number showed increased mean response time with increased numbers of distractors (mean 1742ms, SD 77.952; mean 1919ms, SD 84.723 and mean 2002ms, SD 85.257 with 11, 17 and 23 distractors respectively).

Analysis of group showed slower mean response times for the post-stroke relative to healthy participant group in both saliency condition (high salience: mean 1443ms, SD 100.414 and mean 748ms, SD 44.907 respectively; low salience: mean 22219ms, SD 129.085 and mean 1556ms, SD 57.728 respectively).

Concerning target-hand congruency interaction with group, healthy participants showed no target-hand congruency effect ($F(1,14) = 1.754, p = 0.207, \eta^2 = 0.111$). Post-stroke participants also showed no target-hand congruency effect ($F(1,2) = 9.712, p = 0.089, \eta^2 = 0.829$) (Fig. 5).

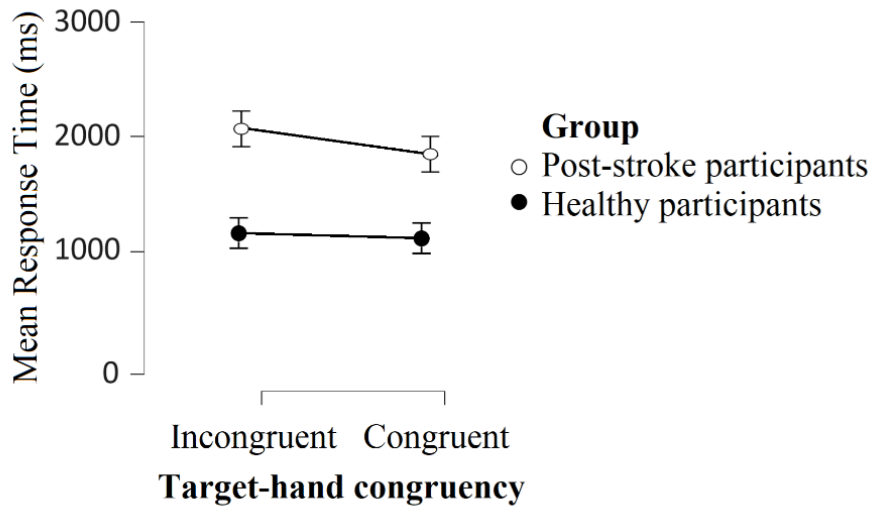


Figure 5. *Mean response times in levels with distractors (i.e., from 2 to 7) organised according to target-hand congruency, in post-stroke with sequelae vs healthy controls groups. Presentation of the mean response times (in milliseconds) in successful trials with target emerging in the two alternative positions. On the Y-axis the mean response time. On the X-axis the two possible target position (i.e., hemifield contralateral vs. ipsilateral to the playing hand). The error bars show the 95% confidence interval. Outlined circles represent post-stroke participants with USN at the gold standard tests; black-filled circles represent healthy controls.*

The present analysis revealed no statistically significant target-hand congruency effect in either the healthy control group or the post-stroke group with visual USN.

While the control group showed a negligible effect, the post-stroke group demonstrated a large effect size despite failing to reach conventional statistical significance. This is likely attributable to the very small sample size ($N = 3$). With such a limited number of participants, the statistical power of the analysis is substantially reduced, increasing the likelihood of a Type II error.

Chapter 2

These findings suggest that future research should include a larger sample of post-stroke participants with visual USN to adequately test for group differences in target-hand congruency effects.

Chapter 3

The REAsmash serious game for the post-stroke diagnosis of distractor inhibition: Contrast between immersive and non-immersive virtual reality test versions

Gregorio Sorrentino, Khawla Ajana, Gauthier Everard, Florence Vanhoof, Thierry Lejeune and Martin Gareth Edwards

Published in

European Journal of Physical and Rehabilitation Medicine, April 2025.

DOI: 10.23736/S1973-9087.25.08680-0

Abstract

BACKGROUND: Virtual Reality (VR) Serious Games (SG) offer greater sensitivity and specificity than traditional diagnostics. The playfulness of the serious games reduces stress, enhancing motivation and reliability. We developed immersive (iVR) and non-immersive (niVR) versions of REAsmash, a SG based on Feature Integration Theory (FIT) to assess distractor inhibition attention.

AIM: To verify the transfer of the REAsmash FIT diagnostic properties across VR devices with different degrees of immersion.

DESIGN: Cross-sectional clinical study.

SETTING: Inpatient, outpatient and healthy controls.

POPULATION: Post-stroke and healthy individuals.

METHODS: The REAsmash involves searching for a (target) mole with a red miner's helmet. The target is either presented alone (baseline), or

Chapter 3

presented with distractors (11, 17 or 23) that contrast the target by high or low saliency (moles with blue miner's and horned helmets vs blue miner's and red horned helmets). Stimuli appeared randomly from a 24-molehill grid. Participants (15 with and history of cortical-subcortical stroke and 15 age matched controls) hit the target with their response hand in niVR and with a virtual hammer in iVR. Post-stroke participants used their less impaired hand, controls their dominant hand. ANOVA tested VR type (niVR vs iVR), group (post-stroke vs healthy), saliency (high vs low) and distractor number (11, 17, 23), with the interaction between saliency and distractor number defining FIT. The dependent variable was relative mean response time, calculated by subtracting the mean baseline response time from each response to targets presented with distractors, for each participant. This variable exemplifies the costs to response time cause by the manipulation of independent variables.

RESULTS: We found significant main effects and an interaction for saliency and distractor number, confirming FIT. Group and VR type main effects were significant, with slower responses for post-strokes and for iVR, but with no interactions.

CONCLUSION AND CLINICAL REHABILITATION IMPACT: To evaluate performance across acute to chronic post-stroke phases, diagnostic measures must be transferable between test devices, ensuring compatibility from hospital to outpatient settings. Our results demonstrated that the REAsmash diagnostic properties were consistent across immersive and non-immersive VR, as well as within both groups of participants.

Key words

Immersive Virtual Reality; Non-Immersive Virtual Reality; Distractor Inhibition; Stroke, Rehabilitation; Cognitive Evaluation; Assessment.

Introduction

There are an estimated 80 million disabled stroke survivors worldwide¹⁰¹, making stroke the leading cause of long-term disability in high-income countries². With increased innovations in health care and longer average life expectancy, a 35% increase in stroke prevalence is expected by 2030^{3,4}. Because of these two factors, it is paramount to develop new and improved diagnosis and neurorehabilitation methods for stroke care.

Currently, the estimated prevalence of post-stroke cognitive impairments is uncertain, with estimates varying from 24 to 96%¹⁴¹. Part of this variance is explained by the different domains of cognition that can be affected by stroke. However, another contributor to this variance results from routine evaluation of cognitive deficits being overlooked in most clinics^{47,48}. Even though the literature clearly demonstrates the impact of cognitive deficits on global post-stroke recovery, and makes frequent calls for more comprehensive, precise and routine evaluations of cognition during post-stroke diagnosis of impairments^{18,120}.

The use of Virtual Reality (VR) and Serious Games (SG) methods provide promising reliable tools for cognitive assessment and rehabilitation¹⁴². VR is defined as a computer-generated immersive experience⁵⁶. It ranges from non-immersive (niVR) to fully immersive (iVR)⁵⁶. In niVR, participants typically interact with content via input peripherals (e.g., keyboard, touchscreen or hand tracker) and an output device (e.g., screen or tablet)⁵⁷. Fully iVR generally refers to technology that recreates an interactive three-dimensional and multisensorial experience using a head mounted display (HMD), large screen projection system (SPS) or cave automatic virtual environment (CAVE)⁵⁹. The HMD is a wearable device equipped with two small screens positioned near the eyes, typically within goggles or a helmet. It includes a head-tracking sensor that adjusts the visual display according to head movements, and it has headphones for delivering auditory feedback⁵⁹. The SPSs are large displays that project the virtual environment onto a screen. The CAVE consists of a room featuring four to six screens, which when used with 3D glasses, provide an immersive and continuous

Chapter 3

visualization of virtual spaces. This setup is further enhanced by a head-tracking sensor and speakers to deliver audio stimuli⁵⁹.

SG are games designed with a primary purpose other than pure entertainment, such as education and training¹⁴³. As suggested by Tong et al., specially adapted SG can be leveraged to create an interactive and engaging tool that promotes patient-centered cognitive assessment⁵⁴. The primary objective of a SG using VR for cognitive assessment is to motivate the participant to perform the task. The SG incorporates challenging goals and are fun to play¹⁴⁴. SG promotes maximised user performance (the best ability of the player), increasing test/re-test reliability¹⁴⁵ and allowing the collection of large amounts of digital measurement data, boosting measurement sensitivity and specificity. Furthermore, as for all computerised assessments¹⁴⁶, the possibility of randomising the presentation of the stimuli allows the SG to diminish practice effects, while maintaining control and standardization across individuals.

The impact of the degree of immersion in VR is a topic that is still not fully understood, especially in post-stroke populations. Immediately post stroke, patients tend to have increased anxiety¹²⁸ caused by a change to personal routine and future uncertainty, which typically dissipates with time. Anxiety can moderate user experience when using VR technology¹²⁹. For example, studies on cognitive assessment have demonstrated that VR naïve relative to experienced participants show more difficulties when performing tasks in iVR than niVR, explained by anxiety¹⁴⁷. A similar effect is reported for age, with aged relative to young participants showing more difficulties in iVR relative to niVR¹²⁶, again explained by anxiety. However, despite these results, recent research with iVR on older adults with cognitive decline has shown good acceptance, possibly due to the use of new HMDs that minimise cyber sickness and allow immersive experiences more closely resembling real life¹²⁷. Nevertheless, iVR effects on sense of presence, flow, and the transfer of skills or knowledge to real-world contexts remain a matter of debate in the academic literature¹⁴⁸. Taking the overall results, it may be the case that niVR relative to iVR is better suited to acute and sub-acute post-stroke patients who are naïve in the use of VR technology,

regardless of patients' age, and that with increased time, there becomes no difference in user experience between niVR and iVR, making a transition to iVR possible for sub-acute to chronic patients. This pathway of technology would allow use of niVR in clinical settings, transitioning to the use of iVR in outpatient and home-based settings.

From a broader clinical standpoint, the economic implications of device selection remain a pivotal consideration. In resource-limited regions, as well as within healthcare systems of low- and middle-income countries, the financial investment in diagnostic technologies cannot be overlooked¹⁴⁹. This is particularly relevant given the substantial cost differential, ranging from tens of thousands of euros for niVR devices to mere hundreds of euros for iVR solutions. Our study contributes to the discussion about the appropriateness of choosing one type of VR over another already in the diagnostic field.

Recently we developed the REAsmash¹²⁴, a SG adaptation of the classic fairground and arcade game, Whac-A-Mole. The objective was to create a new assessment tool that systematically evaluates distractor inhibition attention. Although the disruptive effect of distracting stimuli (i.e., irrelevant information⁴¹) has a known impact on performance¹²⁵, with many replications of the effect in the literature³⁹, there is currently no validated diagnosis test for distractor inhibition impairment that is routinely used in clinical practice. The REAsmash aims to address this unmet need. The SG was validated for full iVR with healthy participants (REAsmash-iVR)¹²⁴, and has recently been tested with different groups of post-stroke participants¹³². The REAsmash SG is based on Feature Integration Theory (FIT) by Treisman and Gelade¹²⁵, which contrasted response time performance to two target-distractor contrast conditions. In a high saliency target-distractor contrast condition, the target differed by one salient feature from the distractors (e.g., a red target presented with blue distractors), leading to "parallel search" where the target "pops-out" from the distractors.

This effect shows that attention is directly drawn to the target stimulus. In contrast, in a low saliency target-distractor condition, the target differs from

Chapter 3

the distractors by a conjunction of features (e.g., a red circular target presented with blue circular and red square distractors, with red and circle features shared with the distractors). This condition leads to “serial search”, where the participant spatially scans the stimuli one at a time, attentionally inhibiting the distractor stimuli until they find the target. Treisman and Gelade showed that in parallel search, increasing numbers of distractors did not change response time. However, response time in the serial search condition was influenced by distractor number, with increased numbers of distractors increasing response time. Therefore, the diagnosis criteria for measuring distractor inhibition relies on the interaction effect between salience and distractor number.

The REAsmash aims to replicate the FIT paradigm using gamified animated complex stimuli in both niVR and iVR, showing: (i) overall longer response times to accomplish the task in low compared to high salience conditions and (ii) an interaction effect, with no effect of distractor number for the high salience condition and increased time to find the target with increased distractors in the low salience condition. In earlier preliminary studies using the iVR version (submitted¹³²), post-stroke participants were contrasted to healthy controls. No participants were enrolled in both the preliminary and the study concerned in this article. Post-stroke participants showed particularly pronounced difficulties in low-salience target-distractor levels, where they exhibited substantially prolonged response times and higher rates of errors and omissions. This finding suggests a specific impairment in serial search and distractor inhibition in this population, distinguishing them from healthy controls.

Few studies in the literature have compared the same cognitive task in different degrees of VR immersion, and we found no studies exploring this issue in relation to tests of distractor inhibition.

In our main experiment, we tested a group of post-stroke participants and an age-matched group of healthy controls on the REAsmash presented in niVR and iVR. The main objective was to verify the transfer of the FIT effect across devices with different degrees of VR immersion. We thus

hypothesized to replicate our preliminary research findings, showing a significant saliency by distractor number interaction effect (demonstrating FIT), and no differences, or interactions between use of niVR and iVR (particularly for the diagnostic criteria). As a secondary objective we explored possible differences between groups to investigate possible interactions between VR types (iVR vs niVR), cognitive demand (parallel vs serial research) and groups. Prior to the main experiment described in this paper, we ran a preliminary study on healthy participants playing with both niVR and iVR REAsmash SG, testing possible differences in hand use (dominant vs non-dominant) on outcomes. Our hypothesis was that, because of a consistent neutral starting position (in the center of the playing field), response times, as well as error and omission rates, would not be affected by the hand used.

Materials and methods

Study design

This study uses a cross-sectional clinical study design and followed the STROBE guidelines¹⁵⁰. The protocol was approved by the Saint Luc-UCLouvain clinical ethics committee (Belgium) (2015/10FEV/053) and registered on clinicaltrial.gov (NCT04694833). Details on the design of the study are reported in the following sections.

Participants

To determine the required sample size, an a priori power analysis using G*Power® (version 3.1.9.7) was performed on previous data testing the FIT effect with 60 healthy participants. The power analysis was conducted considering a single group, as the primary objective was to establish the necessary sample size to detect the FIT interaction effect across different VR technologies. This data showed the hypothesised significant interaction between target-distractor saliency contrast and distractor number ($F(2,114) = 117,58$, $p < 0,001$, $\eta^2 = 0,67$), and an effect size (Cohen's f) of 1.425.

Chapter 3

Using these parameters, the G*Power analysis indicated that a total sample size of 4 participants is required to show the FIT effect interaction, with a power of 0.80 for detecting the specified effect size at an alpha of 0.05. For our study, which involved contrasting a group of post-stroke participants with healthy participants, we decided to increase the sample size to 15 participants per group. Retrospectively, a sample size of 15 participants per group was deemed sufficient to detect a significant between-group effect ($\eta^2 = 0.96$).

Post-stroke participants were recruited from the physical medicine and rehabilitation department of the *Cliniques universitaires Saint-Luc* in Brussels and were either currently hospitalised or already discharged. Recruitment took place from December 2022 to March 2024. The post-stroke participants were selected using the following inclusion criteria: (1) adult participants (i.e., minimum age of 18 years old); (2) presence of an ischemic or haemorrhagic first cortical and/or sub-cortical stroke, diagnosed by CT or magnetic resonance imaging and (3) a good understanding of the task instructions. The exclusion criteria were: (1) uncorrected vision deficiencies; (2) MoCA⁴⁶ score less than 20 out of 30 points; (3) presence of other neurological conditions (e.g., major neurocognitive disorder or extrapyramidal disorders) that could bias the outcomes; (4) medication-resistant epilepsy; (5) orthopaedic dysfunction that could influence upper extremity function and; (6) too poor trunk control to sustain the trial. Points (5) and (6) were clinically evaluated by a Physical Medicine and Rehabilitation specialist in the week preceding the VR sessions. The post-stroke group (n=15; 14 males) had a mean age of 58.4 years (SD=12.4; range: 21-71) and a mean height of 175.5 cm (SD=6.5). Most participants were VR naïve (93%), 54% reported the less impaired hand (i.e., the response hand) was their pre-stroke dominant hand. The average time since stroke was 7 months (range: 1-132 months), 7 participants were in sub-acute phase (i.e., within 6 months from the stroke) and 8 in chronic phase, with 12 ischemic and 3 hemorrhagic strokes. Lesions were located on the right hemisphere in 9 participants and on the left in 6, primarily affecting the Sylvian regions. The mean MoCA score was 26.2 (SD=2.4; range: 20-30). Rehabilitation status varied, with 8 participants still undergoing

neuropsychological, occupational, and/or physical therapy at the time of testing.

Healthy controls were recruited between November 2021 and March 2024 through the University of Louvain participation panel and social media groups. The participants were selected using these inclusion criteria: (1) they should have normal or corrected to normal vision and (2) no neurological, psychiatric or orthopaedic disorders potentially affecting compliance or limiting upper limb functionality. Difficulty in understanding French (the language of the task instructions) was an exclusion criterion.

The healthy control group ($n=15$; 7 males) had a mean age of 58.1 years ($SD=14.4$; range: 21-81) and a mean height of 170.3 cm ($SD=8.1$), showing no significant age and height differences to the control group. Although gender ratio was different between groups, we expected no gender effects for FIT (with males and females showing equal ability to inhibit visual distractors). Most participants were VR naïve (86%). Further details, including individual participant data, are provided in Tables 1a and 1b, available as online-only supplementary material. All the participants volunteered to participate in the study, providing written informed consent before participation.

Materials

The ‘REAsmash’ Serious Game (SG) was created using Unity 2019.3 software (in C# language). The REAsmash presented a visual display of 24 molehills displayed in a cartoon-like garden (organized into 6 columns and 4 rows). The grid of molehills was aligned with an active surface of 100 x 50cm in both the niVR and iVR devices. The stimuli presented to participants was organized by 7 blocks of 24 trials (game levels). The participant was instructed to ‘Smash’ (hit) the target stimulus that pseudo-randomly appeared from one of the 24 molehills, making the 24 trials for each block / level. The target stimulus was a mole wearing a red miner’s helmet. In the baseline level 1 trial block, no distractors were presented. In the remaining trial block levels, distractors were presented with the target

Chapter 3

mole. The distractor moles wore different helmets and were used to create high versus low saliency contrasts to the target mole (creating a measure of distractor inhibition demands). In the high saliency target-distractors contrast condition, the target was presented with distractor moles wearing blue helmets (miner's or horned) (levels 2, 3 and 4). In the low saliency target-distractors contrast condition, the target was presented with distractor moles wearing either blue miner's or red horned helmets (levels 5, 6 and 7). In the high salience condition, the target differed from the distractors by colour, whereas in the low salience condition, the target differed from the distractors by a conjunction of features (both colour and helmet shape). In each of the two target-distractor salience conditions, 11, 17 or 23 distractors accompanied the target, making stimuli sets of 12, 18 and 24 stimuli (corresponding to levels 2, 3 and 4, and levels 5, 6 and 7; Figure 1).

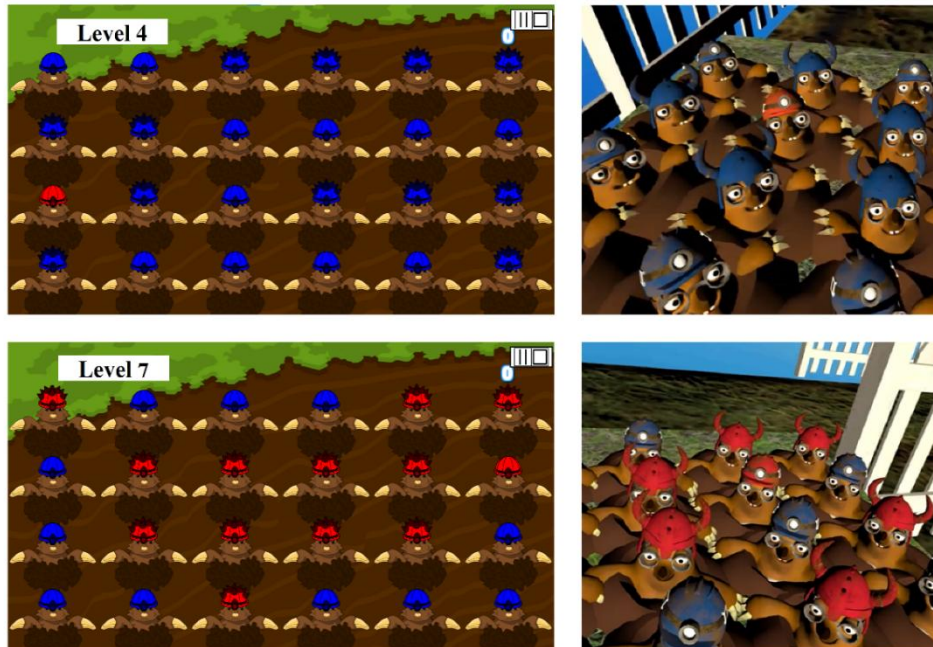


Figure 1. The REAsmash target-distractor search stimuli. Examples of stimuli settings. The upper images show level 4 (high salience) with 23 distractors wearing horned or miner's blue helmets. The lower images show level 7 (low salience) with 23 distractors, wearing red helmets with horns and blue miner's helmets. The two images on the left column represent the stimuli as they appeared in the REAsmash-niVR version of the SG, while the images on the right are taken from the REAsmash-iVR SG.

The REAsmash-niVR ran on the REAtouch® (Axinesis®) interactive medical device. This was composed of a touch-sensitive screen (43", 95 x 53 cm) incorporated in a motorized structure that allowed customised screen lifting and inclination tilting. The REAtouch® provides multisensory and real-time performance feedback and is designed to allow uni- or bi-manual interaction by direct hand-contact with the screen. The hardware for the REAsmash-iVR consisted of an immersive VR headset (Oculus Quest 2) and one Oculus Quest motion controller. When the virtual hammer hits the mole helmet, Oculus Quest 2 provides a real-time performance acoustic

Chapter 3

feedback, and the respond controller vibrates. The experiment was monitored through a live stream from the Oculus App (Figure 2).

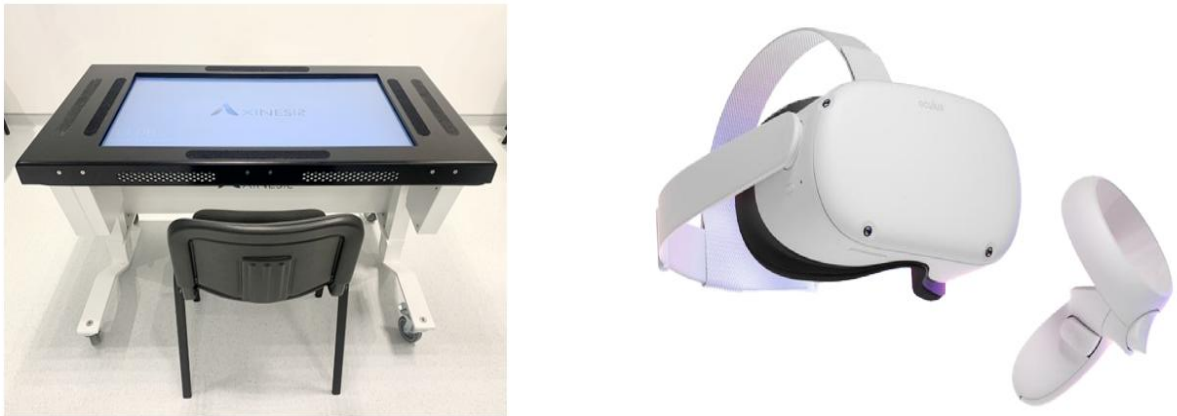


Figure 2. The non-immersiveVR and immersiveVR devices. *On the left, the REAtouch® (Axinesis®), a touch-sensitive 43" screen tablet with multisensory and real-time performance feedback. The height and inclination of the touch-sensitive screen can be adjusted. In the present study the inclination was the same as that presented here (i.e., 0°). On the right, the Oculus Quest 2®, the immersive VR headset (with a per-eye resolution of 1832×1920 , and a refresh rate of 120 Hz), and one Oculus Quest motion controller (left or right according to the response hand), used for manual responses.*

Procedure

The study was run in controlled laboratories at the Cliniques universitaires Saint-Luc of Brussels (Belgium) and at the University of Louvain (UCLouvain). All sessions were conducted by a PMR specialist, who was the intervention provider for the project. Before the study, participants were given instructions regarding the experimental design, and they were invited to sign a consent form. They were informed that they could withdraw from the study at any time.

When playing the REAsmash-niVR SG, participants were asked to sit on a chair positioned in front of the REAtouch® and aligned with the central sagittal axis of the interactive touch-sensitive screen (see Figure 2), with their feet placed on the ground. The screen was adjusted to a suitable height, allowing the participant to make responses to all parts of the screen, and making their position comfortable for the experiment. The touch-sensitive screen was presented at a horizontal angle of zero degrees relative to the ground. Participants were instructed, by means of a superimposed message on the playing field that was also verbally spoken by the software, to touch the target as quickly as possible with their playing hand. To begin each trial, the participant had to touch an “X” stimulus that appeared at the mid-lower edge of the touchscreen. This was used to provide a consistent starting point prior to each trial response. After touching the start position, the trial would begin.

The format of the REAsmash-iVR SG experiment matched that of the REAsmash-niVR SG. Participants were invited to sit on a chair, wearing the iVR headset and hold the controller in their response hand. Multimodal (i.e., written and verbal) instructions were played at the beginning of the SG, instructing the participants to hit the target stimulus as fast as they could, using a virtual hammer that was controlled with the iVR controller. As in the case of niVR, the height of the playing field could be adjusted for comfort, allowing participant to interact with all parts of the display. Before each trial, to provide a consistent starting point, two red squares were displayed floating in front of the participants, aligned with the central sagittal axis of the playing field and placed on the edge nearest to the player (matching the location of the X in the niVR display). One square had a pictogram of an eye, and the second had a pictogram of a hammer. The participants had to simultaneously fixate on the eye-square and place the hammer on the hammer-square to initiate each trial. When the participant's head and virtual hammer positions were correctly located, the two red squares turned green, and the trial began (Figure 3). Note that the iVR used head tracking to measure head rather than eye position.

Chapter 3

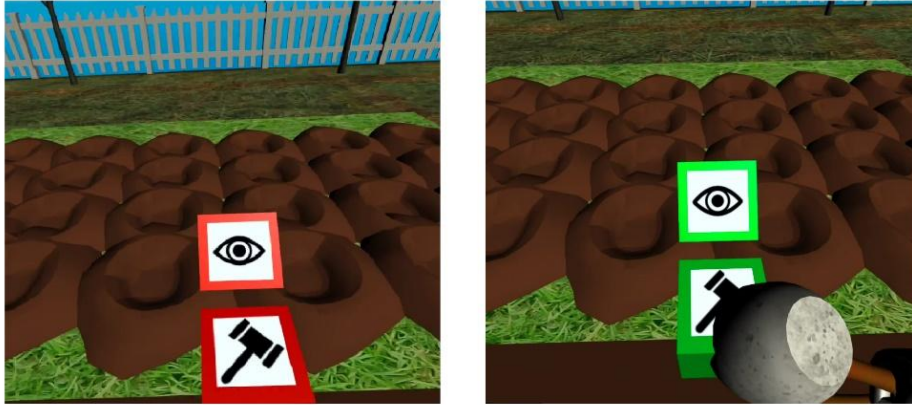


Figure 3. *The starting position in iVR. When the cubes with the eye and hammer pictogram turned from red (left frame) to green (right frame), both the position of the head and the response hand were correctly placed and the trial was initiated.*

In the case of participants in wheelchairs, the wheelchair was appropriately positioned aligning the participants to the same playing conditions as the other participants. A 10-trial practice session was used to familiarize participants with the devices before each session. A 20-second rest period was provided between each game level. The 7 levels were run from easy to difficult (levels 1-7 in sequence).

All mole stimuli appeared for a maximum time of 7 seconds. If the participant made no response, the trial was considered as an omission, while if they responded to a distractor stimulus, the trial was considered as an error response. If a correct response was made within 7 seconds, the trial was terminated, and the next trial was initiated.

The playing hand, in the case of post-stroke subjects was the less impaired hand. In current clinical cognitive diagnosis tests, post-stroke individuals are frequently asked to use their less impaired (ipsi-lesional) hand for making responses. This is carried out to reduce the influence that motor impairments have on the interpretation of cognitive impairments.

Prior to the main experiment, we conducted a preliminary experiment on healthy participants to verify the hand used had no effect on response times. In this preliminary study, 10 healthy participants (average age 60 years, SD 10.6) performed the REAsmash with both hands, randomising the hand order. These data are presented in the Results section.

All participants performed the two versions of the REAsmash (niVR and VR). The order of the two sessions were randomised and took place with a maximum of one week separation to minimize potential cross-platform practice effects.

Outcomes

The following behavioral outcomes were measured in this paper, constituting the dependent variables.

For the preliminary experiment, the primary outcome was absolute mean response Time (AT), consisting of the mean response time between target appearance and manual response (i.e., the virtual hammer hits the mole helmet) in successful trials.

For the main experiment, we introduced Relative mean response Time (RT) for successful trials. This outcome was calculated by subtracting the mean response time of baseline level (Level 1) from the mean response times recorded in Levels 2 to 7. RT highlights the temporal cost of different task conditions, isolating the cognitive demands of distractor inhibition from individual variability in absolute response time. The dependent variables RT was introduced to control for individual variability intra- and inter-group.

In both experiments, two further outcomes were collected: (i) Error Rate, defined as responses made to distractor stimuli instead of the target and (ii) Omission Rate, defined as the failure to respond to the target within the 7-second time limit. Both error and omission rates were calculated as proportions out of the total number of trials for each condition.

Chapter 3

Data analyses

Data analyses were performed using SPSS 27.0 (IBM®). The normality of the data was investigated using the Shapiro-Wilk test, and then repeated measures ANOVAs. Post-hoc analyses were performed with Bonferroni corrections for multiple comparisons.

For the preliminary experiment on healthy participants contrasting hand use, the dataset consisted of 3360 trials (i.e., 7 levels x 24 trials x 10 participants for the dominant and non-dominant hand) for each VR type. The independent variables were hand (dominant vs non dominant) and game level (7 levels), with a separate ANOVA for each VR type (as the intention here was to isolate differences for hand used).

For the main experiment, we focused on target-distractor saliency and number of distractors, comparing groups and type of VR. Each participant group was composed of a total dataset of 5040 trials (i.e., 7 levels x 24 trials x 15 participants x 2 VR type). The independent variables were VR type (iVR vs niVR), target-distractor saliency (high vs low), distractor number (11, 17 and 23) and group (post-stroke vs healthy controls).

Availability of Data and Materials

The datasets used during the current study are openly available in the open data archive of University of Louvain (<https://dataverse.uclouvain.be/dataset.xhtml?persistentId=doi:10.14428/DVN/OM0TIM>).

Results

The post-stroke group included 1 female, and all participants were right-handed, with an average age of 58.4 years (SD 12.4). The control group included 8 females and 4 left-handed participants with an average age of 58.1 years (SD 14.4) (see Tables 1.a and 1.b). The post-stroke and control groups were mean age matched, with a t-test showing no significant difference in age between the two groups ($t(28) = -.125, p = .902$).

No participants withdrew before the end of the study. No adverse events occurred during the experiment. The sessions were well tolerated and overall described as non-stressful and engaging. No participants asked to stop the experiment prematurely or to extend the rest periods.

The preliminary experiment testing hand differences in healthy participants

Concerning the preliminary experiment, the niVR dataset, there were 12 omissions (0.3%), 11 errors (0.3%), 5 anticipatory responses (0.1%) (i.e., responses imitating in less than 250 ms) and 48 outliers (1.4%) (defined by a three standard deviation confidence interval). In the iVR dataset, there were 24 omissions (0.7%), 19 errors (0.6%), 0 anticipatory responses and 67 outliers (2%).

The ANOVA on RT for the niVR dataset showed a significant main effect of game level, $F(6,54) = 300.7$, $p < 0.001$, $\eta^2 = 0.97$, but no significant main effect of the response hand $F(1,9) = 0.235$, $p = 0.639$, $\eta^2 = 0.03$, and no interaction between level and response hand $F(6,54) = 0.340$, $p = 0.913$, $\eta^2 = 0.04$. Similarly, the ANOVA for the iVR dataset showed a significant main effect of game level, $F(6,54) = 238.347$, $p < 0.001$, $\eta^2 = 0.96$, but no significant effect for response hand $F(1,9) = 0.001$, $p = 0.982$, $\eta^2 = 0.000$, and no significant interaction $F(6,54) = 0.364$, $p = 0.899$, $\eta^2 = 0.04$. Therefore, these data showed that starting from a consistent central position, the response showed no differences between hand used to respond to a spatial target.

The main experiment

For the post-stroke group, in niVR, there were 71 omissions (1.4%), 10 errors (0.2%) and 4 anticipatory responses (0.07%), and in iVR, there were 89 omissions (1.8%), 30 errors (0.6%) and 0 anticipatory responses. For the healthy control group, in niVR, there were 9 omissions (0.2%), 7 errors (0.1%), 5 anticipatory responses (0.1%) and 37 outliers (0.7%), and in iVR, they made 29 omissions (0.6%), 15 errors (0.3%), 0 anticipatory responses and 51 outliers (1%).

Chapter 3

The ANOVA for RT showed significant main effects of target-distractors saliency $F(1,28) = 630.15$, $p < 0.001$, $\eta^2 = 0.96$, distractor number $F(2,56) = 82.62$, $p < 0.001$, $\eta^2 = 0.75$, VR type $F(1,28) = 99.18$, $p < 0.001$, $\eta^2 = 0.78$ and group $F(1,28) = 12.25$, $p = 0.02$, $\eta^2 = 0.96$). Multiple interactions were also statistically significant: (i) saliency and distractor number, $F(2,56) = 79.26$, $p < 0.001$, $\eta^2 = 0.74$; (ii) VR type and saliency, $F(1,28) = 58.19$, $p < 0.001$, $\eta^2 = 0.68$; (iii) VR type and distractor number, $F(2,56) = 8.31$, $p < 0.001$, $\eta^2 = 0.23$ and (iv) VR type, saliency and distractor number $F(2,56) = 7.13$, $p = 0.002$, $\eta^2 = 0.20$ (Figure 4). No significant interaction was found between VR type and group $F(1,28) = 2.19$, $p = 0.150$, $\eta^2 = 0.07$, and there were no other significant interactions.

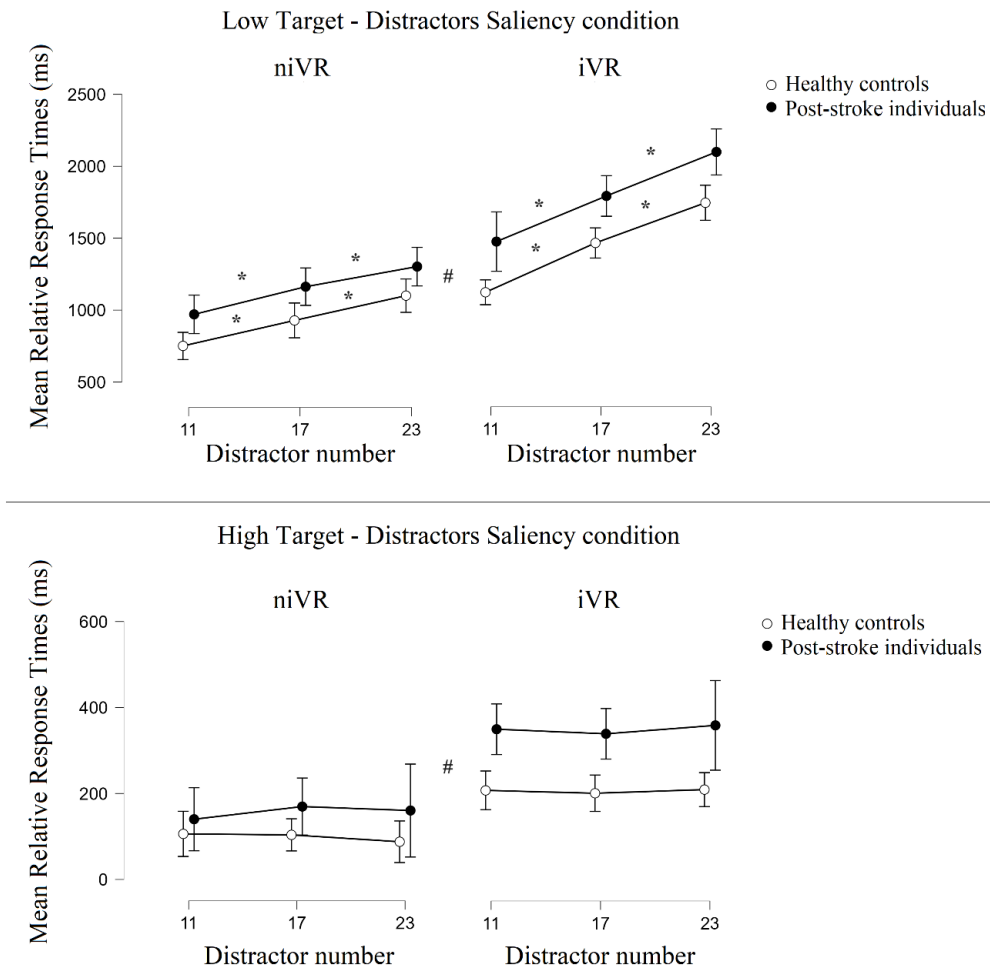


Figure 4. Mean relative response time for independent variables of target-distractor saliency, number of distractors and group (milliseconds). The upper plots show the low saliency conditions while the lower plots show the high saliency conditions. On the left, the results in niVR and on the right, the results of the iVR. The error bars show the 95% confidence interval. Black-filled circles represent post-stroke participants; Outlined circles represent healthy controls. “*” represent significant main effect for distractor number; “#” represent significant main effect for VR type. The results for both VR types showed the classic FIT effect, with the number of distractors showing no differences for high target-distractors saliency, but a

Chapter 3

significant increase in mean relative response time with increased number of distractors in the low target-distractors saliency. The post-stroke group was significantly slower than the healthy controls group. The iVR responses were significantly slower than the niVR responses (relative to baseline).

We first focus on the interaction between target-distractor saliency and distractor number. To analyse the interaction, we ran two separate ANOVAs for each target-distractor saliency condition (high and low). As predicted, the high saliency condition showed no significant differences for numbers of distractors $F(2,56) = 0.07$, $p = 0.935$, $\eta^2 = 0.002$, whereas for the low saliency condition, there was a significant effect $F(2,56) = 86.198$, $p < 0.001$, $\eta^2 = 0.755$, with RT increasing with increased numbers of distractors ($M = 1081.54\text{ms}$, $SD = 46.86$; $M = 1340.18\text{ms}$, $SD = 58.80$ and $M = 1565.73\text{ms}$, $SD = 50.65$ with 11, 17 and 23 distractors respectively).

We next focus on the three-way interaction between VR type, target-distractor saliency and distractor number (i.e., the FIT effect versus VR type), which encompasses the interaction effects between VR type and saliency, and VR type and distractor number. Separate ANOVAs were run for each saliency condition, testing distractor number and VR type. For the high saliency target-distractors condition there was a significant effect of VR type ($F(2,28) = 24.95$, $p < 0.001$, $\eta^2 = 0.471$), with slower responses for iVR relative to niVR. No other statistically significant results were found for high saliency condition. For the low saliency target-distractors condition, there was a significant effect of numbers of distractors $F(2,56) = 86.20$, $p < 0.001$, $\eta^2 = 0.75$ (showing increased RT with increased numbers of distractors) and VR type $F(1,28) = 112.05$, $p < 0.001$, $\eta^2 = 0.80$ (showing slower relative response time for iVR than niVR), as well as a significant interaction between VR type and numbers of distractors $F(2,56) = 8.90$, $p < 0.001$, $\eta^2 = 0.241$. We further separated the low saliency condition by distractor number and found significant main effects of VR type in all the three distractor conditions ($F(1,28) = 41.63$, $p < 0.001$, $\eta^2 = 0.598$; $F(1,28) = 74.88$, $p < 0.001$, $\eta^2 = 0.728$ and $F(1,28) = 117.94$, $p < 0.001$, $\eta^2 = 0.808$ for 11, 17 and 23 distractors respectively) with longer RT in iVR than niVR ($M = 860.80\text{ms}$, $SD = 47.17$ vs $M = 1302.27\text{ms}$, $SD = 67.15$;

M = 1045.53ms, SD 53.69 vs M = 1634.83ms, SD 79.70 and M = 1201.75ms, SD 56.64 vs M = 1929.71ms, SD 64.57 with 11, 17 and 23 distractors in niVR relative to iVR respectively).

Discussion

From a general perspective, this paper adds new understanding on the use of VR in SG for improving the cognitive diagnosis of distractor inhibition, for which there is currently no objective clinical diagnosis test used in clinical practice.

Firstly, the preliminary study on 10 healthy participants confirmed that the design of our SG and the choice of introducing a consistent neutral and central starting position in both types of VR minimised differences between the hand used for the task. This was demonstrated by the data showing no performance difference between use of the dominant compared to non-dominant hand. However, the potential problem with this decision is that some patients will make responses with their pre-stroke dominant hand, whereas others will now make responses with their pre-stroke non-dominant hand, potentially causing differences in response efficacy. To improve diagnosis tests requiring manual responses, we suggest that a consistent starting position is necessary to eliminate subjacent differences that are not stroke-related, such as making responses with the former dominant compared to former non-dominant. Such differences of hand dominance are removed with the central starting position.

The main objective of this paper was to verify the transfer of the FIT effect between iVR and niVR versions of the SG, contrasting post-stroke participants with healthy age-matched controls. For this purpose, we used the dependent variable of RT. This modified measure (relative to the usual AT) adds a second new value to the diagnosis literature proposing a strategy to minimise potential differences introduced by different VR devices, where one requires direct hand interaction, and the other uses an iVR controller.

For the main objective of the study, the contrast between types of VR (iVR vs niVR), we found a significant main effect of VR type, with RT slower in

Chapter 3

iVR than niVR. We also found interactions between VR type and the FIT effect. The interaction is likely explained by increasingly greater F ratios, all being significant, with increasing numbers of distractors in low saliency condition for both VR types. Post-hoc analyses demonstrated the FIT effect in both types of VR, as explained above, but also a consistent effect of slower RT for iVR than niVR for contrasts in saliency and distractor number, with none of the interactions showing more effects. These results suggest that the degree of VR immersion has increased cognitive cost. Currently, there is no literature comparing the same cognitive inhibition task in different degrees of VR immersion. However, our results are in line with Makransky et al^{151,152}, who demonstrated reduced performance in immersive compared to non-immersive environments, arguing that immersive VR adds extraneous cognitive load (i.e., increased task demands relative to the individual's cognitive capacity¹⁵³). This may be explained by the iVR creating a more absorbing experience than niVR.

A final interesting value of the present study was the significant effect of group, but with no interactions between group and the other variables. Although the purpose of this article was not to validate the REAsmash as an assessment tool, this result is particularly interesting in this respect. The REAsmash seems able to maintain the FIT characteristics in high and low cognitive load VR environments, replicating results from healthy participants. The stability of the FIT effect, irrespective of the speed of response, the two devices, and for different populations, makes the REAsmash an ideal candidate for a clinical evaluation tool. Overall, these results support the ability to transfer diagnosis tests between two different devices. This consistency in diagnostic characteristics allows a strategy where one could use niVR in the acute to sub-acute phase post-stroke, transitioning to iVR in the sub-acute to chronic phase. This allows for increased neurorehabilitation possibilities for post-stroke individuals, potentially extending rehabilitation to telemedicine methods, and use of iVR in the home or in outpatient settings. In the case of extended neurorehabilitation, the REAsmash can be used as an independent test to verify progress in treatment.

The present study has some limitations. The preliminary study conducted on 10 healthy participants provides limited evidence, and its findings should not be generalized to the broader population without further validation. Additionally, while the results suggest that the starting position effectively reduces variability related to handedness in this specific task, contrasting findings in the literature warrant caution in extending these conclusions beyond the context of this study.

We decided not to segregate participants by post-stroke phase, resulting in a single group of post-stroke participants in different recovery phases (from one month to 11 years since the stroke). Since the results suggest a higher cognitive load in iVR than niVR, further research on REAsmash should investigate differences caused by post-stroke phase (sub-acute vs chronic), to verify whether niVR is more suitable for the sub-acute phase.

The absence of proper haptic and force feedback in the iVR setting is a limitation, particularly for the stroke group, where the lack of feedback may have influenced task performance by reducing sensory-motor integration demands. Future iterations of this study could explore the inclusion of haptic technologies in iVR, which might better leverage the immersive medium's capabilities and provide additional insights into user responses.

This study did not match participants by gender as no effects for the primary task based on FIT have been reported in the literature, demonstrating that cognitive and attentional processes are unlikely affected by gender differences¹²⁵. Therefore, controlling gender was considered unnecessary for the scope of this research. Nonetheless, we acknowledge that gender differences might provide valuable insights for other contrasts, such as use of technology. Future research should balanced gender representation to better understand cognitive performance and task engagement.

Another limitation is that we included both VR naïve and non-naïve participants. As our study used a cross-sectional clinical design, not having prior experience with VR might have influenced the outcome results¹⁴⁷.

Chapter 3

Future studies which aim to clinically validate the REAsmash as a diagnostic tool should take this into account.

Observation during the sessions led to the realisation that trunk control, especially in iVR, played an important role in task execution. The iVR sessions induced the participant to maintain postural control of the response upper limb. As there is no true contact between the hammer and mole's helmet, no external forces stopped the movement once the helmet had been hit. The participant therefore had to actively control the movement throughout the entire trial. Even when the response hand was the less impaired (as in our experiment), the trunk played an important role in balancing forces and stabilising posture, but also in the execution of the movement, which includes torsion movements of the trunk to reach the furthest targets. Future studies on the REAsmash would benefit from the introduction of a trunk control measure, such as a rating scale (e.g., the Trunk Impairment Scale^{139,140}) or an objective motion tracking measure of trunk movement, integrated into the assessment.

Conclusions

As we hypothesised, and in accordance with what has been theorised in the literature, we demonstrated that while the type of VR immersion influenced response time, the diagnostic criteria of the REAsmash test was unaffected by type of VR. To successfully evaluate cognitive performance across different post-stroke phases, it is important to develop measures that are transferable between test devices, providing diagnostic compatibility from hospital to outpatient settings (for example, from bulky niVR to wearable and more ecological iVR devices). Our results demonstrated that the diagnostic properties of REAsmash were consistent across the two types of VR, as well as within both groups of participants. The REAsmash is a useful new assessment tool able to systematically evaluate distractor inhibition attention in both niVR and iVR. Future SG with search tasks should consider the transferability of the test diagnostic criteria for different types of VR immersion, providing more value to patient clinical care.

Author Contributions

Gregorio Sorrentino designed the presented study, analyzed the data, interpreted the results and wrote the paper; Khawla Ajana, Gauthier Everard, Thierry Lejeune, Martin G. Edwards created the REAsmash, interpreted the results of the present paper, and helped write the paper; Florence Vanhoof interpreted the results of the present paper and helped write the paper. All authors contributed to editorial revisions in the manuscript. All authors read and approved the final manuscript. All authors have participated actively in the work and accepted responsibility for all aspects of the work.

Acknowledgment

We thank Julien Sapin (AXINESIS) and Stephane Grade for providing help and support with the REAtouch® and the immersive virtual reality version of our serious game.

Conflict of Interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Supplementary Material

Tables for online version

Table I.a The demographic characteristics of the post-stroke subjects.

ID	Sex	Age (years)	Height (cm)	VR naive	Was the response hand the dominant one before the stroke?	Stroke Phase	Stroke type	Brain lesion side	Brain lesion location	Current spatial attention impairment	History of cognitive impairment	Current Rehabilitation
P1	M	69	172	Yes	Yes	Sub-acute	Hem	Right	Sylv+Deep	No	Yes	Nps+Ergo+Phys
P2	M	65	176	Yes	No	Sub-acute	Isch	Left	MCA	No	Yes	Nps+Ergo+Phys
P3	M	62	183	Yes	Yes	Sub-acute	Isch	Right	MCA	Yes	Yes	Nps+Ergo+Phys
P4	M	53	173	Yes	No	Sub-acute	Isch+Hem	Left	Sylv	No	Yes	Nps
P5	M	65	180	Yes	No	Chronic	Isch	Left	MCA	No	Yes	No more
P6	F	52	166	Yes	No	Chronic	Isch	Left	Sylv	No	Yes	Phys
P7	M	52	178	Yes	Yes	Chronic	Isch	Right	Sylv	Yes	Yes	No more
P8	M	62	164	Yes	No	Chronic	Hem	Left	MCA	No	Yes	No more
P9	M	64	181	Yes	Yes	Chronic	Isch	Right	Sylv	No	Yes	Phys
P10	M	54	180	Yes	Yes	Chronic	Isch+Hem	Right	Sylv	No	Yes	No more
P11	M	21	172	No	Yes	Sub-acute	Hem	Right	Sylv	No	Yes	Nps+Ergo+Phys
P12	M	60	182	Yes	Yes	Sub-acute	Isch	Right	Sylv	No	Yes	Nps+Ergo+Phys
P13	M	71	173	Yes	No	Sub-acute	Isch	Left	MCA	No	No	Phys
P14	M	66	178	Yes	Yes	Sub-acute	Isch	Right	MCA	Yes	Yes	Nps+Ergo+Phys
P15	M	60	184	Yes	No	Sub-acute	Isch	Left	Sylv	No	No	Phys

F = Female, M = Male; Isch= Ischemic, Herm= Hemorrhagic; MCA= Middle cerebral artery, Sylv= Sylvian Segment of MCA; MoCA=Montreal Cognitive Assessment²⁵; Nps= neuropsychological therapy, OT= Occupational therapy, PT = Physiotherapy.

Table I.b The demographic characteristics of the healthy controls.

ID	Sex	Age	Height (cm)	VR naïve	Dominant hand
HS1	M	48	180	No	Right
HS2	F	21	168	Yes	Left
HS3	M	45	178	Yes	Left
HS4	F	54	166	Yes	Left
HS5	F	67	174	Yes	Right
HS6	F	69	160	Yes	Right
HS7	M	51	181	Yes	Right
HS8	M	75	178	Yes	Left
HS9	M	65	173	Yes	Right
HS10	F	55	164	Yes	Right
HS11	M	61	180	Yes	Right
HS12	F	64	165	Yes	Right
HS13	F	64	163	Yes	Right
HS14	F	81	164	Yes	Right
HS15	M	52	184	No	Right

F = Female, M = Male.

Chapter 4

REAsmash-ET: A methodological framework for combined cognitive and motor assessment through eye-tracking and kinematic metrics in immersive VR search-and-reach task

Gregorio Sorrentino, Martin Gareth Edwards, Nicolò Baldini, Magda Mustile, Thierry Lejeune and Gauthier Everard³

Published in

Journal of NeuroEngineering and Rehabilitation, December 2025.

DOI: 10.1186/s12984-025-01844-0

Abstract

BACKGROUND: Virtual Reality (VR) Serious Games (SGs) can provide a functionally relevant framework to capture cognitive and motor dynamics. Their interactive and engaging nature improves compliance, measurement reliability and allows for more frequent evaluations. Additionally, VR SGs enable the parallel collection of multiple types of data within a single session. We present REAsmash-ET, an immersive VR adaptation of the REAsmash SG, grounded in Feature Integration Theory (FIT) and integrating eye-tracking (ET) and upper limb kinematic (UL) analyses. REAsmash-ET introduces a novel methodological framework for the simultaneous assessment of attentional and motor functions in VR.

METHODS: REAsmash is an interactive search-and-reach task designed to elicit structured visual exploration and UL motor responses under varying target-distractor saliency conditions. Custom algorithms extract metrics on visual search strategies and UL motor efficiency. Three age groups of adult healthy participants (n=15 each) were included to test the feasibility and

Chapter 4

methodological consistency of the task and its metrics. Relative Response Time (RRT) and ET metrics were analyzed using ANOVA with factors: age group (20-39, 40-59, 60-80 years), target-distractor saliency (high vs. low), and number of distractors (11, 17, 23). Kinematic metrics were analyzed by age group and response hand (dominant vs. non-dominant).

RESULTS: REAsmash-ET differentiated visuomotor performance across task conditions. RRT and ET metrics showed significant effects of saliency, number of distractors, and their interaction, consistent with FIT. Age-related differences emerged in both RRT and visual search efficiency. Kinematic analyses revealed slower and less efficient movements in older participants, with effects of hand dominance. The results support the robustness and feasibility of REAsmash-ET as a methodological framework.

CONCLUSIONS: The results support the robustness and internal consistency of REAsmash-ET as a methodological framework for the integrated assessment of visual attention and UL motor control in immersive VR. The task's ability to capture visuomotor variability and its multidimensional approach highlight its potential for future research and clinical applications in both healthy and clinical populations.

REGISTRY NUMBER: This study was registered at ClinicalTrials.gov (NCT04694833).

Keywords

Eye tracking; Virtual reality; Spatial attention; Distractor inhibition; Cognitive evaluation; Upper limb kinematics; Cognitive-motor interaction.

Background

Context

With around 80 million survivors worldwide, stroke is the primary cause of long-term disability in developed countries² and the third cause of long-term disability worldwide¹. Stroke prevalence is expected to further increase in the next years^{3,4}. Despite improvements in post-stroke care, survivors typically present a combination of long-term cognitive and motor deficits¹³.

Estimates of cognitive impairment among stroke survivors remain uncertain and highly variable, with prevalence in the acute / sub-acute stages ranging from 24 to 80%⁴⁴, partially explained by a lack of consensus in assessment protocols¹⁴¹. Comprehensive cognitive assessments are not systematically performed on a routine basis in clinics^{47,48}, due to the limited number / availability of neuropsychologist specialists trained for cognitive assessment. Access to stroke-specific cognitive rehabilitation services in community settings is also limited, further reducing cognitive follow-up chances in the post-discharge phase¹⁵⁴.

Furthermore, clinical presentations of cognitive impairments in stroke survivors typically involve multiple cognitive functions (such as visuospatial abilities, inhibition, memory, executive functioning^{105–109}) with great variability in survivors' cognition and brain lesion profiles¹⁵⁵. This variability further complicates assessment and, as a consequence, the rehabilitation process^{13,110}.

Classical neuropsychological testing procedures, such as paper-and-pencil tests, often diverge from real-world demands, as they rarely provide complex and dynamic scenarios, and are susceptible to practice effects³³. Computerized cognitive assessments can provide quantitative data such as speed and response consistency³³, however, they typically require long administration times, and often lack motivational appeal^{33,38}. Furthermore, computerized cognitive assessments are usually conducted in 2D environments that do not reflect real-life interactions. In this context, assessment of visuospatial attention appears to be more sensitive when

Chapter 4

performed in immersive virtual reality (iVR) compared to traditional paper-and-pencil tests¹⁵⁶. Gamifying computerized cognitive assessments can improve participant engagement, while maintaining the accuracy of quantitative data collection¹⁵⁷.

Motor deficits, intended as loss or limitation in muscle control or reduced mobility¹⁵⁸ are well-documented in the literature, affecting approximately 80% of stroke survivors¹⁵⁹. Consistent evidence indicates that over 75% of survivors experience persistent Upper Limb (UL) impairment during the chronic stage¹⁶⁰. UL impairments can result in difficulties with reaching and grasping abilities¹⁶¹, limiting individuals' autonomy to accomplish Activities of Daily Living (ADLs)¹⁶². For UL motor evaluation, the literature recommends several tests (e.g., Fugl-Meyer Assessment¹⁶³, Box and Block Test¹⁶⁴, and Action Research Arm Test¹⁰²)¹⁶⁵. These tests align with the International Classification of Functioning, Disability and Health (ICF)¹⁶⁶ framework, serving as reliable and valid tools in post-stroke assessment¹⁶⁷. These tests are widely used worldwide, providing a reliable picture of the functional condition of the UL affected by stroke¹⁶⁷. However, despite their strong measurement properties^{168,169}, most of these clinical assessments exhibit floor and ceiling effects¹⁷⁰.

These effects can be attributed to several well-known limitations¹⁷¹: (i) limited sensitivity. Most assessments use ordinal scales, which may not detect minor yet clinically significant improvements during rehabilitation¹⁷²; (ii) lack of movement quality analysis. Traditional tests focus on task completion but do not provide detailed insights into movement characteristics such as speed, smoothness, or coordination¹⁷³. These kinematic parameters could help distinguish between active restorative movements and compensatory strategies¹⁷⁴ and (iii) observer-dependent variability. Some assessments rely heavily on clinical observation, introducing subjectivity and inter-rater variability, which can affect the consistency and reliability of assessment outcomes¹⁷⁵.

Integrating kinematic analysis can help address these limitations, enhancing the precision and objectivity of motor function evaluation¹⁷⁶. However,

introducing these technologies into clinical practice faces challenges related to clinical utility, including high costs, the need for specialized equipment and trained personnel, time-consuming data processing, and the absence of standardized, easy-to-use protocols suitable for everyday healthcare settings¹⁷⁷. Furthermore, kinematic metrics are typically not collected during training (in-game), but only during specific assessment tasks performed outside the training sessions¹⁷⁸.

Differences in addressing motor and cognitive deficits may be related to the traditional approach of managing cognitive and motor impairments as distinct issues, with motor recovery often being the primary goal¹⁷⁹. However, the combined presence of motor and cognitive disabilities further reduces individual autonomy in ADLs and quality of life, increasing caregiver dependency and reducing social participation¹⁸⁰. These findings highlight the critical need for reliable and routine cognitive assessments and neuropsychology practice in post-stroke care, as frequently advocated in the literature¹⁸¹. Increasing evidence points to a strong connection between cognitive and motor functions, supporting the importance of integrating cognitive assessment with quantitative (kinematic) evaluation of residual motor abilities in stroke¹⁸². A large body of studies has shown that cognitive functions, such as attention and visuospatial abilities¹⁹, play a crucial role in guiding motor performance, motor learning, and overall recovery¹⁸.

Notably, recent evidence suggests that simulating ADLs in controlled settings provides a meaningful framework for assessing cognitive-motor interaction, as these tasks require the simultaneous engagement of motor control, attention, executive functioning, and memory¹⁸³.

The first challenge for both neuroscientific research and clinical settings is thus to propose a consistent, objective, and reliable assessment of both cognitive and motor impairments, integrated into the overall rehabilitation process to facilitate the development of personalized and effective rehabilitation programs, while ensuring clinical utility through feasible, accessible, and time-efficient tools that can be easily implemented in routine clinical practice.

Chapter 4

Through the integration of different technologies including Virtual Reality (VR), Eye-Tracking (ET) and motion tracking sensors, Serious Games (SGs) offer a novel interactive approach to assess both cognitive and motor functions^{61,184}. SGs are, by definition, games (i.e., gamified tasks) designed with a primary purpose beyond entertainment⁵¹, often aimed at facilitating learning, incorporating challenging tasks to keep participants motivated⁵². They enable the collection of extensive quantitative (e.g., response times and number of fixations) and qualitative data (e.g., task strategies or behavioral patterns inferred from gaze trajectories) during task execution, increasing the potential to capture subtle motor and attentional differences by capturing real-time information on performances⁵³. Additionally, as with computerized assessment¹⁴⁶, the randomization of stimulus presentation can help minimize practice effects while ensuring consistency and standardization across individuals.

REAsmash-ET is a SG we developed for investigating and objectifying visual search through the integration of ET technology into our original SG, the REAsmash¹²⁴. REAsmash-ET enables precise measurement of cognitive visual-spatial attention interactions within compact 3D Regions of Interest (ROIs) representing the stimuli in a fully immersive VR environment. The REAsmash-ET presents stimuli in a horizontal playing field, matching the orientation of traditional paper and pencil tests, and the orientation of a consistent part of the ADLs¹⁸⁵. From a technical perspective, this orientation presents challenges in fine-tuning the algorithm for raw ET data interpretation, as both accuracy and precision are strongly influenced by the spatial distance of the stimulus (i.e., whether it is located close to or far from the observer relative to the horizontal axis)¹⁸⁶. This paper aims to address these challenges, demonstrating suitability for capturing and analyzing gaze behavior in dynamic, horizontally structured settings.

We aim to propose our serious game as a tool for studying different components of visuospatial attention involved in a target search-and-reach task, including distractor inhibition and working memory, reflected by the tendency to fixate repeatedly on distractors or return to them during visual exploration.

We further leveraged the built-in features of VR systems to analyze motor performance data, including speed, precision, and smoothness of the UL response.

Before introducing the REASmash-ET, we describe an overview of the two main technologies employed in this project: iVR and ET.

Fully immersive VR (iVR)

Definition of fully iVR

Fully iVR generally refers to technologies designed to create an engaging interactive, three-dimensional, multisensory environment by employing Large Projection Systems (LPSs), Cave Automatic Virtual Environments (CAVEs) or Head-Mounted Displays (HMDs)⁵⁹. LPSs consist of large screens that project the virtual environment onto a display surface. A CAVE is a room equipped with four to six projection screens that, when viewed with 3D glasses, create a continuous and immersive visual experience. This setup is further improved with head-tracking sensors and speakers to provide audio stimuli⁵⁹. HMDs are wearable devices equipped with integrated screens, head-tracking sensors, and auditory feedback systems⁵⁹. Their strong clinical utility relies on their portability, ease of use, and minimal setup requirements, which make them well-suited for hospitalized patients, outpatient care, and potentially even home-based rehabilitation^{62–64}. In contrast to other immersive VR systems that require complex and expensive infrastructures, HMDs offer a practical and scalable solution for routine clinical applications.

Interest of fully iVR in Neurorehabilitation

Fully iVR enables the design of safe, fully immersive 3D virtual environments, typically difficult or impossible to replicate within a clinical setting, such as street-crossing or virtual supermarkets¹⁸⁷. These environments can provide a multisensory experience, combining visual, auditory, and motor stimulation, which allows for customized levels of challenge and engagement tailored to individuals with varying severities and

Chapter 4

types of deficits^{92,188}. The field of motor assessment has played a pioneering role in integrating new technologies into clinical practice¹⁸⁹. A growing body of literature supports the use of iVR for rehabilitative purposes in post-stroke, highlighting its potential to enhance engagement, functional outcomes, and therapy adherence⁷⁰.

Interest of iVR in Assessment

iVR technologies have been demonstrated as valuable tools for evaluating complex and/or multiple tasks^{190,191}. In particular, the introduction of reliable kinematic measures during iVR tasks reinforces traditional practices by providing objective data¹⁹². Kinematic analysis is now a well-recognized methodology for quantifying motor-related metrics¹⁹³. Fully iVR-based cognitive assessment showed greater accuracy than conventional paper-and-pencil methods¹⁹⁴. HMDs allow for the consistent recreation of ideal testing conditions, independent of the real environment, enabling excellent session standardization with minimal disruption from real-world stimuli and excellent clinical utility^{62–64,195}. Modern devices allow for the integration of various types of data, including behavioral outcomes, kinematic measures and gaze metrics. These data streams can be used independently (e.g., kinematics to assess motor execution or gaze metrics to evaluate attention and decision-making) but can also be combined to explore the interaction between cognitive and motor domains in ecologically valid, task-based scenarios⁶⁵. This characteristic makes these tools particularly valuable in complex assessment settings, such as post-stroke, where different types of deficits often coexist and are interdependent.

Eye-tracking

The elementary components of gaze movements and definition

of Eye-Tracking

The elementary components of gaze movements while free viewing, reading or visual searching for a target are classically distinguished by fixations and saccades¹⁹⁶. Fixations occur when the gaze remains relatively stable for a

sufficient period, allowing cognitive processing of the stimulus upon which the gaze persists⁶⁷. Saccades, on the other hand, are ballistic movements of the eye between two fixation points, during which limited cognitive interaction is possible⁶⁷. There is a third category of eye macro-movements named ‘smooth pursuit’, which occurs when a visual pursuit of a moving stimulus is required¹⁹⁷.

ET technology refers to the measurement of eye movements to understand where an individual’s visual attention is directed⁶⁶. It is based on the principle that eye movements are used to bring the visual area to be explored into the center of the visual field (i.e., the foveal region), where the highest concentration of photoreceptors enables detailed visual processing^{68,198}.

Various types of eye-tracking technologies are available today. A broad classification based on device setup divides ET technologies into two groups: remote and wearable systems. Remote ET systems are typically used in screen-based studies, enabling natural computer interaction while collecting gaze data without physical contact¹⁹⁹. However, while they simplify data handling, remote systems are restricted to fixed locations and may produce gaps or artefacts if participants move their heads excessively²⁰⁰.

Wearable or head-mounted ET systems, such as headbands, glasses, and helmet-mounted devices often feature a secondary scene camera capturing the participant’s field of view²⁰¹. These devices enable free movement during experiments and are valued for their binocular vision accuracy⁴¹. Mobile ET technologies are particularly suitable for real-world studies, although tracking peripheral gaze is less precise, and gaze data must be recorded in the scene camera’s coordinate system due to the lack of a fixed reference frame¹⁹⁹.

An innovative system is represented by iVR-ET HMDs²⁰², a particular type of mobile device with ET systems built into HMD for fully iVR. As recently suggested by Kaise et al.¹⁹⁴, this novel technology provides an

Chapter 4

unprecedented opportunity in visual exploration, allowing the capture of detailed and accurate temporal and spatial data cross the entire visual field while allowing for full-body movements improving ecological validity.

Interest of ET in neurorehabilitation

ET is a well-established technology in the field of cognitive neuroscience³¹ and offers significant potential in neurorehabilitation due to its ability to track and analyze visual attention in real time and across different types of tasks. Studies using ET have been used for assessment in peri-personal (i.e., within arm's reach)^{203–205} and extra-personal (i.e., beyond arm's reach) spaces^{206,207} paving the way for studies that co-investigate eye-hand interaction. In terms of stimuli, the literature reports wildly different setups, including elementary geometrical shapes²⁰⁸, everyday photographs^{209,210} and videos²¹¹, and more complex stimuli²¹². Different tasks have been employed, such as reading tasks²¹³, free viewing²⁰⁹, and visual search tasks²¹⁴. In the neurorehabilitation field, these types of tasks can be fine-tuned to target specific cognitive functions, including spatial and sustained attention, distractor inhibition, and working memory, increasing real-world applicability through ecological design.

Interest of ET in assessment

ET technology provides a valuable tool for the assessment of visual attention by measuring parameters such as the number and distribution of fixations^{194,215}, promoting a deeper understanding of cognitive and motor interactions⁶⁵. Additionally, ET presents a non-verbal, less cognitively demanding approach for monitoring disease progression in individuals with cognitive deficits⁶⁵.

ET technology demonstrated its validity in various experimental setups, allowing researchers to assess attentional mechanisms across different contexts and task demands in controlled and naturalistic environments²¹⁶. Furthermore, emerging evidence²¹⁷ indicates that ET data aligns closely with established cognitive evaluation methods, suggesting its potential as a tool for assessing severity and monitoring recovery in neurological

conditions. Despite advancements in ET technology, its adoption in clinical settings remains limited²¹⁸.

REASmash-ET

Our research team developed REASmash²¹⁹, a SG adaptation of the classic fairground and arcade game Whac-A-Mole built within a structured paradigm that provides an advanced gamified adaptation of a well-established cognitive paradigm based on Treisman and Gelade's Feature-Integration Theory (FIT) of attention¹²⁵. FIT distinguishes between high- and low-saliency target-distractor conditions. In high target-distractors saliency, the target is prominent among the distractors and attention is directly drawn to the target stimulus through pre-attentive bottom-up "parallel search"³⁷. In low-saliency conditions, individual stimuli need to be recognized as distractor stimuli and inhibited prior to target detection. This process is defined by "serial search"³⁷. Parallel search times remain unaffected by distractor number, whereas serial search times increase with increased distractor number due to the need for more individual distractors to be inhibited.

The primary objective of REASmash was to evaluate the impact of target-distractor salience on visual search efficiency during a structured search-and-reach task, with a focus on visuospatial attention and distractor inhibition measures. To this end, we analyzed behavioral outcomes including error and omission rates and response time for successful trials (see Materials section). The test supports adjustable saliency conditions and has demonstrated cognitive stability when transitioning from classical 2D stimuli to complex 3D cartoon-like animated VR presentations²²⁰. The iVR version integrates UL kinematic tracking and has been shown to enable precise motor performance evaluation^{132,221}.

Previous research on visual exploration has predominantly employed non-immersive VR, focusing on static panoramas^{209,222,223} or 2D visual search tasks^{215,224–229}. These studies indicate that fixation duration is influenced by target-distractor similarity, perceptual difficulty, and stimulus density, with

Chapter 4

similarity increasing fixation time and salience capturing attention. The REAsmash-ET aims to extend this knowledge by proposing, for the first time, ET measurements of visual search during a fully iVR SG, replicating the FIT and without body movement restrictions.

In the following sections, we present the REAsmash-ET methodological framework, including a detailed explanation of the tasks as well as the strategies for processing ET and UL kinematic data. We also provide descriptive ET and motor performance data across the three age groups.

Materials and Methods

REAsmash SG

The REAsmash^{124,132,220} was developed using Unity 2019.3 in C# and featured a cartoon-like 3D garden within a VR environment. The garden contains 24 molehills (6 columns and 4 rows) placed on an active playing surface of 150×100 cm. The task was built on a Whac-a-mole game that is widely known and intuitively understood thereby facilitating accessibility even for individuals with cognitive or comprehension difficulties. A cartoon-style was adopted to minimize both the emotional impact of a game that could otherwise appear violent and the risk of cybersickness^{230,231}. The number of stimuli was defined based on the playing field size and stimulus dimensions, which allowed a maximum of 24 items (1 target and 23 distractors). From this configuration, two additional levels were created with progressively fewer distractors (17 and 11), thereby providing a controlled manipulation of distractor number and saliency across game levels (consistent with FIT). In total, seven levels were implemented: one baseline level with no distractors and six experimental levels crossing two target-distractor saliency conditions (high vs. low) with three distractor set sizes (11, 17, and 23). This structure allowed for systematic modulation of task difficulty while maintaining experimental control and ensuring sufficient data points to detect both within- and between-subject variability. Moreover, the seven-level configuration provides an optimal trade-off between ability to capture performance changes and overall task duration, making it suitable

for future clinical applications.

The task was designed to assess participant response times and accuracy in identifying a target stimulus, a mole wearing a red miner's helmet. The target stimulus appears pseudo-randomly, appearing once from each molehill (24 positions) during each of the seven trial levels, with each game level composed of 24 trials. In the baseline condition (level 0), no distractors are presented, whereas in the high-saliency target-distractor contrast conditions (levels 1 to 3), the target appears alongside distractor moles wearing blue miner's or horned helmets. In the low-saliency contrast conditions (levels 4 to 6), distractors wear either blue miner's helmets or red horned helmets, sharing a conjunction of features with the target (Figure 1). Across levels one to six, 11, 17, or 23 distractors accompany the target, creating stimulus sets of 12, 18, or 24 elements, respectively, with 2, 3, or 4 stimuli per column. In high-saliency contrast levels, blue miner's and blue horned helmet distractors are equally distributed (i.e., 6, 9, and 12 per type in the 3 levels). In the 3 low-saliency levels, blue distractors with horns are replaced by red distractors with horns. We use the collider engine from Unity to detect responses. Every region of interest (i.e. the hammer, the target and the distractors) is matched to a 3D collider, and a response is defined by the collision between the hammer and target or distractor.

Chapter 4



Figure 1. Target-distractor search stimuli. On the left a frame from level 3 (i.e., high target-distractor salience condition) with 23 distractors wearing horned or miner's blue helmets and, on the right, level 6 (i.e., low target-distractor salience) with 23 distractors, wearing red helmets with horns or blue miner's helmets.

VR equipment

Participants were immersed in the virtual environment using an HMD (model: HTC Vive Pro Eye[®], nominal field of view $\approx 110^\circ$ according to manufacturer specifications; effective horizontal field of view $\approx 98^\circ$ as reported in the literature²³², with a per-eye resolution of 1440×1600 pixels) and one hand-held controller. Participants interacted naturally with the scene, without body movement restrictions, by means of a virtual 3D hammer operated using the controller. The HTC Vive Pro Eye[®] uses two fixed infrared stations to create a calibrated tracking environment. These base stations emit structured infrared signals, which are detected by sensors on the HMD and controller to ensure accurate spatial positioning. The HTC Vive Pro Eye[®] provides eye-tracking accuracy of $0.5\text{--}1.1^\circ$ at 120 Hz^{233(p)}, with empirical validation showing mean accuracy $\approx 1.23^\circ$ and RMS precision $\approx 0.62^\circ$ ²³⁴. Tracking via SteamVR of the Vive Pro Eye[®] controllers in static conditions has shown spatial errors on the order of a few millimeters to about a centimeter, depending on axis and setup^{235,236}. The HMD was connected to an Alienware[®] x15 R2 laptop, which acted as the primary computing unit, managing software execution. This setup allowed

real-time monitoring of the participant's field of view on the laptop display while ensuring stable system performance. Previous validation work has shown that the HTC Vive Pro Eye[®] provides high precision tracking with low latency (~22 ms), but that absolute positional accuracy can be affected by changes in the reference plane after temporary loss of tracking²³⁵.

Procedure

Before the experiment, participants received written and verbal instructions. They were then seated on a standard four-legged office chair without wheels or armrests, equipped with an HTC Vive Pro Eye[®] and a controller in their response hand. Participants were asked to remain seated throughout the VR session. The proximal edge of the playing surface was located approximately 20 cm in front of the player's eyes in the orthogonal projection, with an eye-playing field center distance of 75cm (see Figure S1 and Table S1 in the supplementary material for further details about visual angle subtended by the playing field and angular separation between stimuli).

They were allowed to lean forward from the backrest, while remaining seated with both feet on the ground. Eye-tracking calibration was performed using the built-in VIVE Pro Eye[®] procedure, and assisted by the experimenter. On-screen messages guided the participant to wear the headset in the correct position, adjust the interpupillary distance, and follow a moving dot with their gaze as prompted by the system.

Prior to each trial, two red squares, aligned with the center of the playing field, appeared in front of the participant. One square contained an eye pictogram and the other contained a hammer pictogram. To initiate each trial, participants were required to fixate on the eye-square and position the virtual hammer on the hammer-square (Figure 2). Once correctly aligned, the squares turned green and disappeared, signaling the start of the trial. This procedure ensured consistent starting coordinates of both gaze and hammer prior to each trial response. At the beginning of the SG, participants were instructed to hit the target stimulus as quickly as possible with the

Chapter 4

virtual hammer while ignoring the distractors. The response hand had to be the same for all game levels. Once the 7 game levels were completed, the task was repeated with the other hand following a 5-minute pause. The response hand order was randomized.

Stimuli were presented for a maximum duration of seven seconds, with omissions recorded if no response was made, and errors recorded if the participant struck a distractor instead of the target. A correct response was defined as the virtual hammer colliding with the target within the seven-second time window, terminating the trial and initiating the next trial. Participants completed a 10-trial practice session to familiarize themselves with the VR environment, and a 10-second rest period was provided between each trial block (level). The experiment progressed from the easiest condition (no distractors) to the most difficult (23 low-saliency distractors). The full session, including all trial blocks and breaks, lasted approximately 20 minutes per hand.

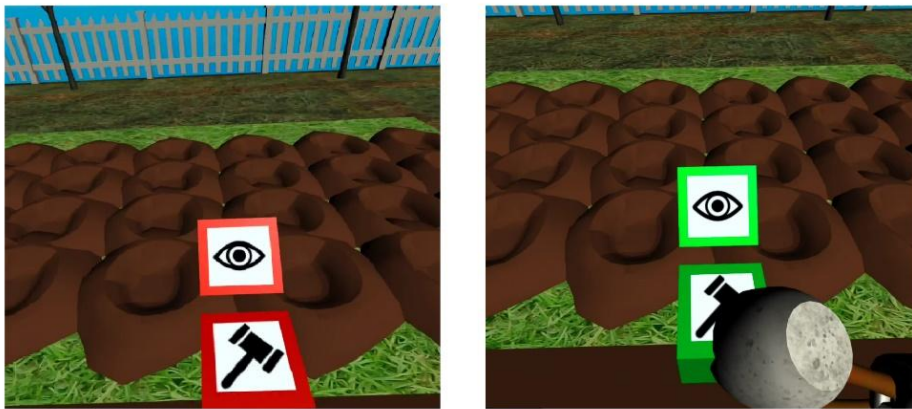


Figure 2. The starting position. Before each trial, the participants viewed the 24 empty molehills and two reference squares, one with an image of an eye that they had to fixate, and one with an image of a hammer, on which they placed their virtual hammer. This enabled a consistent starting point for each trial.

Outcome measures were organized into three domains: (i) task performance, including Relative Response Time (RRT), omission rates, and error rates;

(ii) eye-tracking, including cumulative and mean fixation time on distractors, as well as the number of capture and re-capture fixations; and (iii) upper limb kinematics, including mean and peak velocity, smoothness (SPARC), and coefficient of variation of velocity. This structured framework enabled the parallel assessment of attentional and motor performance within the same immersive VR task, while the following sections detail the feature extraction strategies for ET and UL data.

Eye-Tracking data processing strategy: the semi-adaptive

dispersion-threshold approach

Raw ET data were tracked with the integrated ET system of the HTC Vive Pro Eye[®]. The HMD recorded head position and gaze point relative to the 3D colliders of the VR stimuli at a sampling frequency of 50 Hz. The stimuli represented the ROIs. ET data were recorded from the start of each trial (i.e., when the participant reached the initial position and the two squares turned green and disappeared) until the trial ended (i.e., manual response or end of the 7 seconds allowed per trial). The spatial and temporal positions of head and gaze points constituted the raw ET dataset, stored as “CSV” files on the headset's hard drive for each participant.

To study gaze behavior, we employed a revised version of the dispersion-threshold algorithm by Llanes-Jurado et al.²³⁷. Starting from the original algorithm²³⁷, we first resolved coding bugs related to the computation of gaze vectors²³⁸ and then implemented further refinements to improve data accuracy and robustness (explained below). The original dispersion-threshold algorithm analyses consecutive gaze points according to fixed Angular Dispersion (A_D), where A_D is defined as the angle between two gaze vectors originating from the eyes and reaching two consecutive gaze points. Depending on the distance (d) between the eyes and the stimuli, a fixed A_D can lead to variations in Linear Dispersion (L_D), defined as the linear distance between two consecutive gaze points (Figure 3). This consideration implies a major limitation to the application of fixed A_D for our task (or any tasks to stimuli oriented on the horizontal plane) where

Chapter 4

ROIs are spatially compact (13x16cm) and vary in retinal size according to d from less than 0.5 to 1.5 meters.

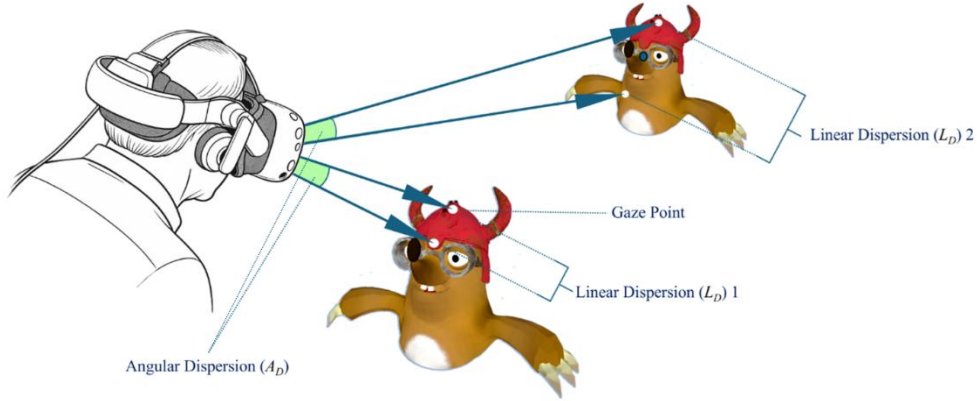


Figure 3. Variation in Linear Dispersion (L_D) at constant Angular Dispersion (A_D). The white dots indicate two consecutive gaze points on a distractor. Angular Dispersion (A_D) is defined as the angle (in green) between two gaze vectors (blue arrows) originating from the eyes and extending to the respective gaze points. The illustration demonstrates that, with a constant A_D between gaze points, the Linear Dispersion (L_D) between the two dots can greatly vary depending on the distance between the observer and the stimulus. In this example, L_{D1} refers to the dispersion on a closer distractor (first row), whereas L_{D2} corresponds to a more distant distractor (fourth row) from the participant's perspective.

To increase the accuracy of gaze data interpretation in our task, we implemented a semi-adaptive A_D approach. Specifically, different A_D values were applied within predefined d ranges, ensuring that gaze points were spatially analyzed under a consistent L_D while accounting for variations in eyes-ROI distance.

Basing our calculations on anthropometric norms of human height and proportions²³⁹, we derived d for each ROI as $d = \sqrt{d_{\perp}^2 + h^2}$, here $d_{\perp}$

represents the orthogonal distance between the eyes and the stimuli ROI and h is the height difference between the eyes and the ROI. Our analysis was centered on the position of the mole helmets, which served as the distinguishing feature among the stimuli (Figure 4).

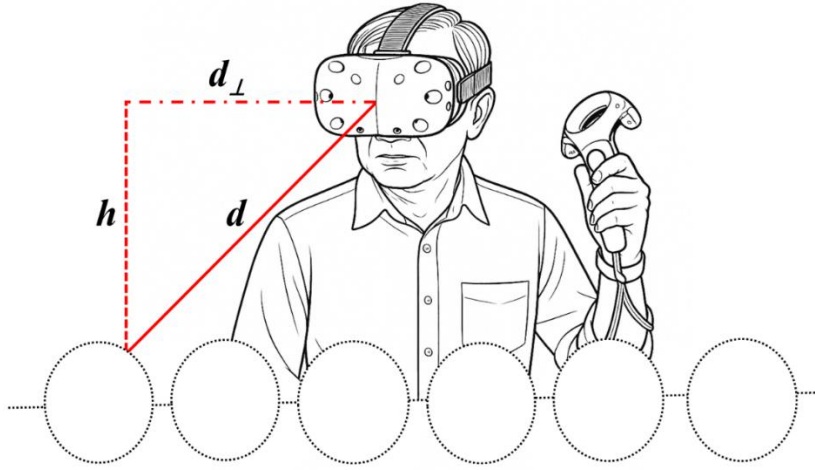


Figure 4. Computation of eyes-ROI distance. Graphical 3D representation of d computation, with $d_{\perp}$ representing the orthogonal distance between the eyes and each ROI and h the height difference between the eyes and the ROI. The virtual objects (i.e., the playing field and the moles) are schematically represented with dotted black lines.

For the REASmash-ET setting, d was estimated to range from approximately 45 cm to 130 cm according to the ROI position on the playing field. We then divided the playing field into three distinct 8 ROIs zones based on d : (i) proximal; (ii) intermediate and (iii) distal. The average d was approximately 60 cm for the proximal zone, 90 cm for the intermediate zone, and 120 cm for the distal zone (Figure 5).

Chapter 4

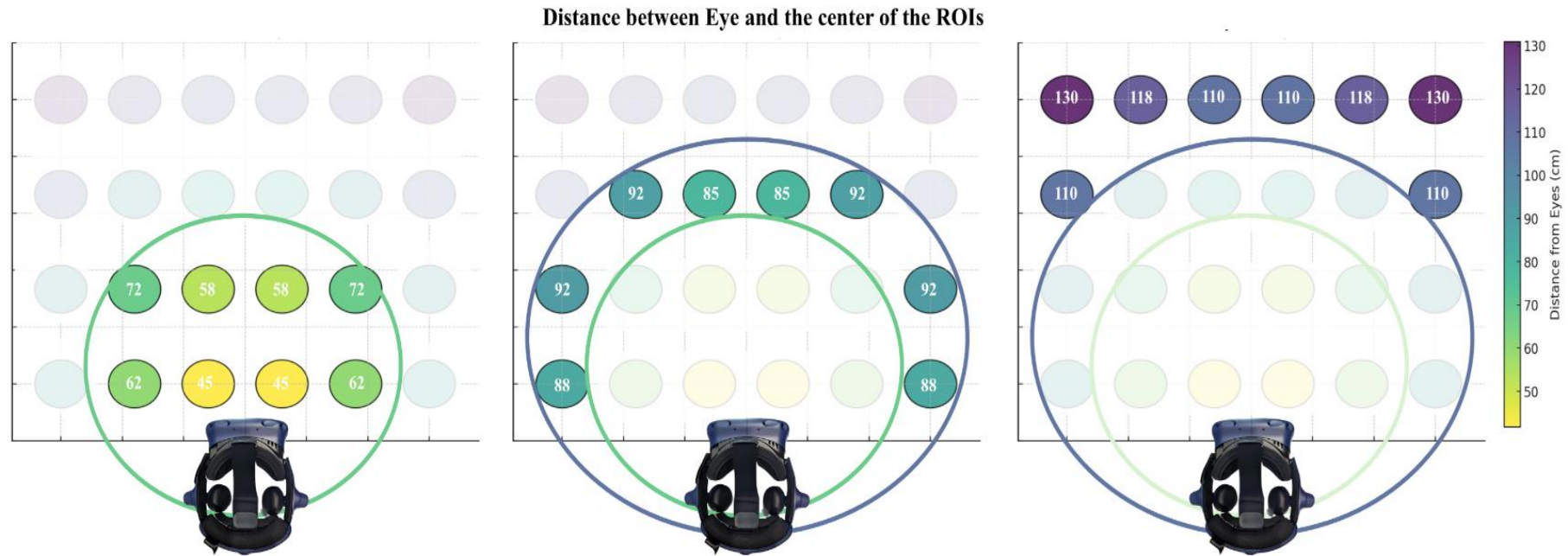


Figure 5. Division of the playing field into three zones according to the average distance between eyes - ROIs. Visual representation of the d (i.e., eyes-ROI distances) in centimeters across the playing field. The three graphics illustrate the classification of ROIs into proximal (a), intermediate (b), and distal (c) zones, based on their estimated distances from the participant's eyes. Colors indicate the measured distance in centimeters, with warmer shades representing shorter distances and cooler shades representing longer distances.

To ensure a constant L_D across the three zones, A_D was calculated as a function of d for a given L_D , using the formula $A_D(d) = 2 \cdot \tan^{-1}(L_D/d)$. We tested the A_D for L_D of 1.5, 2, and 2.5 cm (Figure 6). An L_D in the range of 1.5 to 2.5 cm allows us to discriminate fixations on specific features within the stimuli, such as horns.

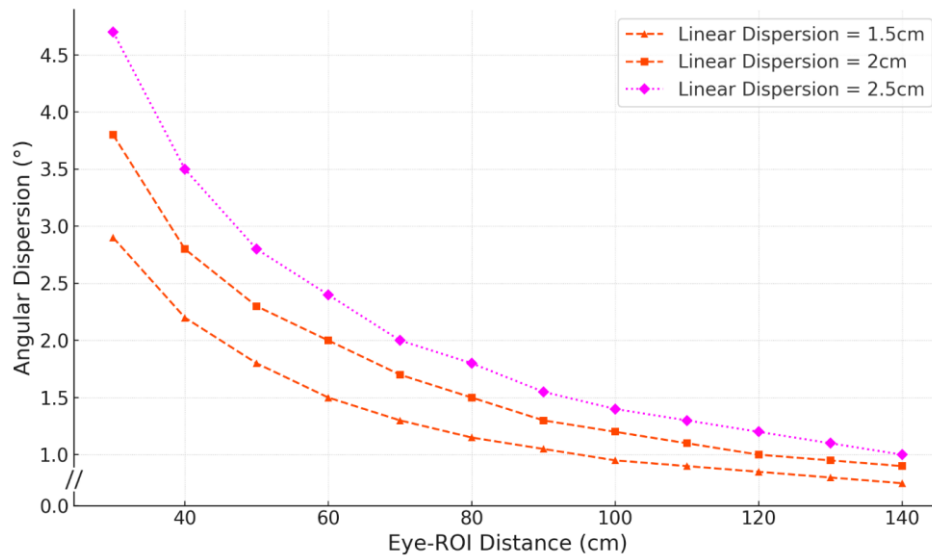


Figure 6. Relationship between Angular Dispersion (A_D) and Eye-ROI Distance (d) across different Linear Dispersion (L_D) conditions. Graphical representation of the relation between A_D , d and L_D . As d increases, the required A_D decreases to maintain a constant L_D with shorter L_D requiring smaller A_D .

The literature suggests A_D between 1° and 2° for visual search tasks similar to the REASmash-ET²⁴⁰. A L_D of 2cm was the only value that fell within the suggested A_D range for d values consistent with our task: an A_D around 2° was needed for an eyes-ROI mean distance of 60cm (proximal zone) and an A_D around 1° was needed for an eyes-ROI mean distance of 120cm (distal

Chapter 4

zone). We then calculated the A_D for an L_D of 2cm with an eyes-ROI mean distance of 90cm (intermediate zone) and found an A_D of 1.3° (Figure 7).

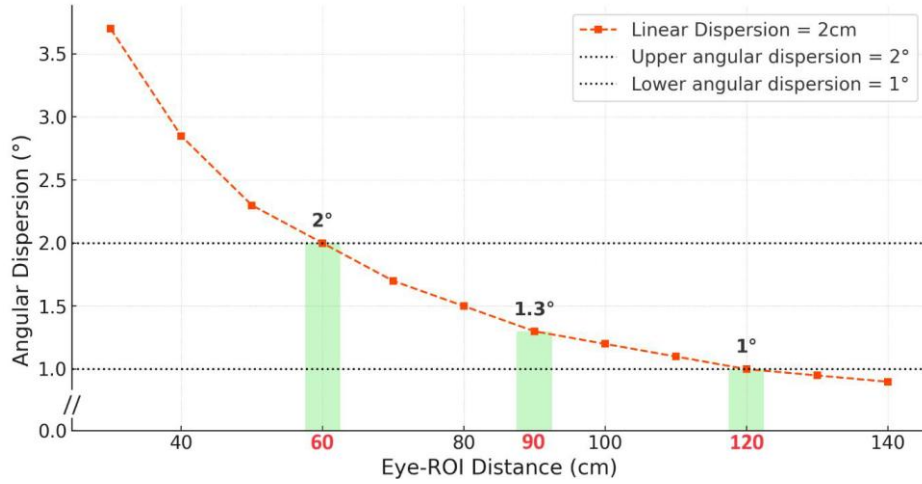


Figure 7. The Angular Dispersion (A_D) for the three zones of the playing field. A L_D of 2cm corresponds to: (i) a A_D of approximately 2° for d of the proximal zone (60cm), (ii) a A_D of approximately 1.3° for d of the intermediate zone (90cm) and (iii) a A_D of approximately 1° for d of the distal zone (120cm).

Following the spatial definition of fixation based on the dispersion of gaze points, we then evaluated fixation using temporal criterion. This is necessary to ensure that the gaze remains sufficiently stable for a minimum duration, allowing cognitive engagement with stimuli located within the foveal region. In accordance with the literature^{240–245}, we set the time threshold at 100ms to exclude false positives and micro-fixations that do not reflect cognitive visual engagement with stimuli. True fixations were gaze points remaining within A_D , whereas saccades were implicitly classified as any gaze movements that did not meet the fixation criteria. For each fixation, duration was calculated as the time difference between fixation onset and offset, corresponding to the time between the first and the last gaze point classified within the fixation. Fixation location was calculated by determining the 3D coordinates of the centroid (i.e., the average spatial position of all gaze points belonging to the same fixation). Fixated objects

were identified by projecting the binocular gaze vector into the virtual scene. When multiple intersections with colliders occurred, the collider with the shortest distance from the gaze origin was selected.

To test the reliability of our ET data, we contrasted distractor fixation duration metrics to behavioral outcomes. This approach permitted to make hypotheses grounded on the FIT to verify the efficacy of REAsmash-ET to detect real cognitive interactions on compact 3D VR stimuli. In high target-distractor saliency trials, the time spent fixating distractors was expected to be close to zero (parallel search). In contrast, in low saliency trials, a positive correlation was expected between the number of distractors and the ET metrics, reflecting visual serial search.

The spatio-temporal computation of the ET data made it possible to study overlapping fixations. We defined capture fixations as two or more consecutive fixations on the same stimulus (i.e., the gaze remains locked on a single object without shifting to others)^{51,75} and re-capture fixations as instances where the gaze returns to a stimulus after having shifted to one or more different stimuli^{209,246,247}. An augmented number of capture fixations likely suggests difficulties in disengaging attention from a stimulus (i.e., a distractor inhibition impairment)^{211,246,248} while an augmented number of re-capture fixations has been interpreted in the literature as a possible marker of spatial working memory impairment^{209,246,247}. Although there is relative consensus regarding the underlying pathological mechanisms of overlapping fixations^{209,211,246}, to date there are no norms regarding these ET metrics. We hypothesized an age effect related to a general decrease in visual exploration efficiency with age²⁴⁹.

The semi-adaptive dispersion-threshold algorithm described here constitutes a general-purpose solution for gaze data analysis in 3D environments with variable eye-to-stimulus distances.

Upper limb kinematic data processing strategy

As for the ET data analyses, we only considered data of successful trials. The 3D position of the controller used for manual responses collected from

Chapter 4

the stimuli appearance to manual response with a sampling rate of 60 Hz. UL kinematic raw data were stored as export files (.csv) on the headset's hard drive for each participant.

This strategy made it possible to study the metrics of UL movement in the temporal window corresponding to response time. Kinematic data were then analyzed using a custom program developed in Python⁹⁹. We first performed a visual inspection of the controller's 3D position over time to ensure data reliability. To reduce acquisition noise, a fourth order Butterworth filter (sampling frequency = 60 Hz; cut-off frequency = 10 Hz) was applied to each dataset. Then, for each consecutive time point, we calculated the Euclidean distance traveled in 3D space and divided it by the time interval (s), to compute the instant velocity signal ($v(t_i)$). For each trial, we calculated in 3D space: (i) Mean velocity; (ii) Peak velocity; (iii) Spectral arc length (SPARC) and (vi) Coefficient of variation of the velocity.

$$(i) \quad \text{Mean velocity} = \frac{\Delta d}{\Delta t}$$

Mean velocity, computed as the mean rate of change position ($\Delta d/\Delta t$), was calculated from the beginning of the trial to the manual response.

$$(ii) \quad \text{Peak velocity} = \max(v(t_i))$$

Peak velocity corresponded to the maximal instant velocity ($v(t_i)$) within a trial.

$$(iii) \quad SPARC = - \int_0^{\omega_c} \left[\left(\frac{1}{\omega_c} \right)^2 + \left(\frac{d\hat{V}(\omega)}{\omega_c} \right)^2 \right]^{\frac{1}{2}} d\omega;$$

$$\text{with } \hat{V}(\omega) = \frac{V(\omega)}{V(0)} \text{ and } \omega_c = \min \left\{ \omega_c^{max}, \min \{ \omega, \hat{V}(r) < \bar{V} \forall r > \omega \} \right\}$$

SPARC is a smoothness metric ranging from $-\infty$ to 0, with higher values corresponding to a smoother movement. It consists in the arc length of the

spectrum of the normalized instant velocity signal ($\hat{V}(\omega)$)^{250,251}. To compute SPARC, we first applied a fast Fourier transform (FFT) to the instant velocity signal in order to obtain its amplitude spectrum as a function of frequency. The spectrum was then normalized by dividing all amplitudes by the maximum amplitude value, scaling the curve from 0 to 1. We computed the arc length of this normalized spectrum within a defined frequency range (ω_c to ω_{max}). Finally, a negative sign was applied to the resulting arc length, so that larger arc lengths (i.e., more irregular and less smooth velocity profiles) correspond to lower SPARC values, while smoother movements yield higher SPARC values.

$$(iv) \quad \text{Coefficient of variation of the velocity} = \frac{SD(v(t_i))}{\text{mean velocity}}$$

Coefficient of variation of the velocity is another smoothness metric ranging from 0 to 100% with lower values corresponding to a smoother movement. The metric is a ratio between the standard deviation (SD) of the instant velocity ($v(t_i)$) and the mean velocity.

Participants

Participants were recruited between July 2023 and April 2024 through the University of Louvain participation panel and social media groups in Belgium and Italy. All the participants gave their written informed consent prior to the beginning of the study. The protocol was approved by the Saint Luc-UCL Hospital-Faculty Ethics Committee (Belgium) (2015/10FEV/053) prior to the initiation of the study and registered on clinicaltrial.gov (NCT04694833). The participants had normal or corrected to normal vision and no neurological, psychiatric or orthopedic disorders potentially affecting compliance or limiting upper limb functionality. The REAsmash-ET instructions were presented in French or Italian depending on the location of testing, and the insufficient understanding of any of these languages was a further exclusion criterion. All participants were naïve to our SG and to iVR.

Chapter 4

To explore differences in age, we divided participants into three age-based groups, each consisting of 15 participants, ensuring a balanced number of left-handed individuals and different genders. Groups were composed as follow: Group 20-39 years, 7 females, 1 left-handed, average age of 24.6 years ($SD = 4.52$); Group 40-59 years, 7 females, 2 left-handed, average age of 49.9 years ($SD = 5.93$) and Group 60-80 years, 6 females, 1 left-handed, average age of 69.6 years ($SD = 3.88$).

Data analyses

All statistical analyses were conducted using SPSS 27.0 (IBM®). The normality of residuals was verified using the Shapiro-Wilk test and in case of significant deviations, data were also log-transformed to assess robustness against potential violations of normality assumptions. Since the results of the ANOVAs were unchanged, we report here the analyses on the untransformed data for clarity. Outlier exclusion was performed using the conventional ± 3 SD rule, applied separately within each age group for each dependent variable (e.g., response times, fixation metrics, kinematic measures). Specifically, trials with values exceeding the mean ± 3 SD of the distribution for that group and variable were removed. The significance threshold was set at $\alpha = 0.05$, and Bonferroni corrections were applied for post-hoc comparisons when appropriate.

Replicating recent publications using REAsmash²²⁰, we selected mean Relative Response Time (RRT) as the main dependent variable for behavioral outcomes. RRT was calculated by subtracting the average response time in the baseline condition (level 0, without distractors) from each response in levels 1 to 6. This measure reflects the additional cognitive cost associated with increasing distractor number and decreasing target-distractor saliency.

To test REAsmash-ET for detecting fixations, we verified the FIT on eye-tracking outcomes. For this purpose, the primary dependent variables were (i) the total cumulative fixation time on distractors per trial and (ii) the mean fixation duration on distractors per trial. Secondary metrics included (iii) the

number of distractors with at least one capture fixation and (iv) the number of distractors with at least one re-capture fixation. Concerning UL kinematics, the dependent variables included (i) mean velocity, (ii) peak velocity, (iii) SPARC and (iv) the coefficient of variation of velocity.

Only successful trials were analyzed for RT, gaze metrics and UL kinematics. Outlier exclusion was performed applying the standard practice of using a three SD confidence interval filter within each age group.

For RRT and gaze metrics, repeated-measures ANOVAs were performed on the dependent variables, with (i) target-distractor saliency (high vs low) and (ii) number of distractors (11, 17, 23) as within-subject independent variables, and (iii) age group (20-39, 40-59, 60-80 years) as a between-subject independent variable.

For kinematic data, the response hand (dominant vs. non-dominant) was chosen as within-subject independent variable. This within-subject factor was intended to assess the ability of kinematic metrics to detect physiological motor asymmetries, even in neurologically healthy individuals. Age group was a between-subject independent variable.

In the presence of significant interactions, separate ANOVAs were conducted within the independent variables concerned by the interaction effect. Due to their low frequency, omissions and errors were reported in the Results section, without further statistical analysis.

Results

All participants completed the experiment. In a general feedback discussion session with the participants after the study, they all described the experimental tasks as non-stressful and engaging. No participants asked to stop the experiment prematurely or to extend the rest periods. No serious and non-serious adverse events, such as cybersickness or epileptic seizures, occurred.

Chapter 4

Behavioral outcomes

Concerning behavioral outcomes, each participant (age) group contributed a total of 5,040 trials (7 levels $\times$ 24 trials $\times$ 15 participants $\times$ 2 hands) for a total data set of 15120 trials. The error and omission rates are presented in Table 1.

Outlier RTs were removed from the successful trial dataset of each group, causing the removal of 62 trials (1.2%) for the 20-39 years group, 92 trials (1.8%) for the 40-59 years group, and 121 trials (2.4%) for the 60-80 years group. No anticipatory responses (i.e., responses faster than 250 ms) were observed in any group (See Table 1).

Table 1. The error and omission rates of the 3 groups.

Age group	Omissions (number, %)	Errors (number, %)	Outliers Removed (number, %)	Anticipatory Responses
20-39 years	8 (0.2%)	5 (0.1%)	62 (1.2%)	None
40-59 years	34 (0.7%)	11 (0.2%)	92 (1.8%)	None
60-80 years	77 (1.5%)	27 (0.5%)	121 (2.4%)	None

The ANOVA for mean RRT demonstrated significant main effects of target-distractors saliency ($F(1,42) = 1897.68$, $p < 0.001$, $\eta^2 = 0.98$) and distractor number ($F(2,84) = 276.46$, $p < 0.001$, $\eta^2 = 0.87$), with longer RTs observed in the low saliency condition and with increasing numbers of distractors. A significant effect of group ($F(1,42) = 19.35$, $p < 0.001$, $\eta^2 = 0.48$) was also found. Multiple interactions were also statistically significant: (i) target-distractors saliency and distractor number ($F(2,84) = 234.56$, $p < 0.001$, $\eta^2 = 0.85$); (ii) target-distractors saliency and group ($F(2,42) = 23.10$, $p < 0.001$, $\eta^2 = 0.52$) and (iii) target-distractors saliency, distractor number and group ($F(4,84) = 3.12$, $p = 0.019$, $\eta^2 = 0.13$) (Figure 8). No other significant main effects and interactions were found.

To analyze the interaction between target-distractors saliency and distractor number, separate ANOVAs were run for high versus low saliency condition.

The ANOVA for the high saliency condition showed no significant differences for numbers of distractors on mean RRT ($F(2,84) = 2.41, p = 0.1, \eta^2 = 0.05$). In contrast, the ANOVA for the low saliency condition showed a significant distractor number effect ($F(2,84) = 281.24, p < 0.001, \eta^2 = 0.87$), with RRT increasing with increased numbers of distractors ($M = 912.01$ ms, $SD 29.15$; $M = 1216.79$ ms, $SD 29.16$ and $M = 1428.05$ ms, $SD 26.50$ with 11, 17 and 23 distractors, respectively).

Concerning the interaction between target-distractor saliency and age group, these analyses demonstrated a significant group effect only in the low saliency condition ($F(2,42) = 24.49, p < 0.001, \eta^2 = 0.54$). No significant group effect was found in the high saliency condition ($F(2,42) = 0.353, p = 0.70, \eta^2 = 0.02$). Mean RRT for high target-distractor saliency conditions were 96.96 ms ($SD 18.42$), 103.93 ms ($SD 18.42$) and 118.42 ms ($SD 18.42$) for age groups 20-39, 40-59 and 60-80, respectively. Mean RRT for low target-distractor saliency conditions were 976.13 ms ($SD 43.86$), 1165.84 ms ($SD 43.86$) and 1411.88 ms ($SD 43.86$) for age groups 20-39, 40-59 and 60-80, respectively, showing increased RRT with age.

For the three-way interaction between target-distractor saliency, distractor number and group (i.e., the FIT effect versus age group), separate ANOVAs per group, confirmed the FIT effect in the three groups ($F(2,28) = 53.25, p < 0.001, \eta^2 = 0.79$; $F(2,28) = 66.62, p < 0.001, \eta^2 = 0.83$ and $F(2,28) = 128.62, p < 0.001, \eta^2 = 0.90$ for group 20-39 years, 40-59 years and 60-80 years, respectively). This interaction shows that the age effect was specifically apparent in the low target-distractor saliency condition.

Chapter 4

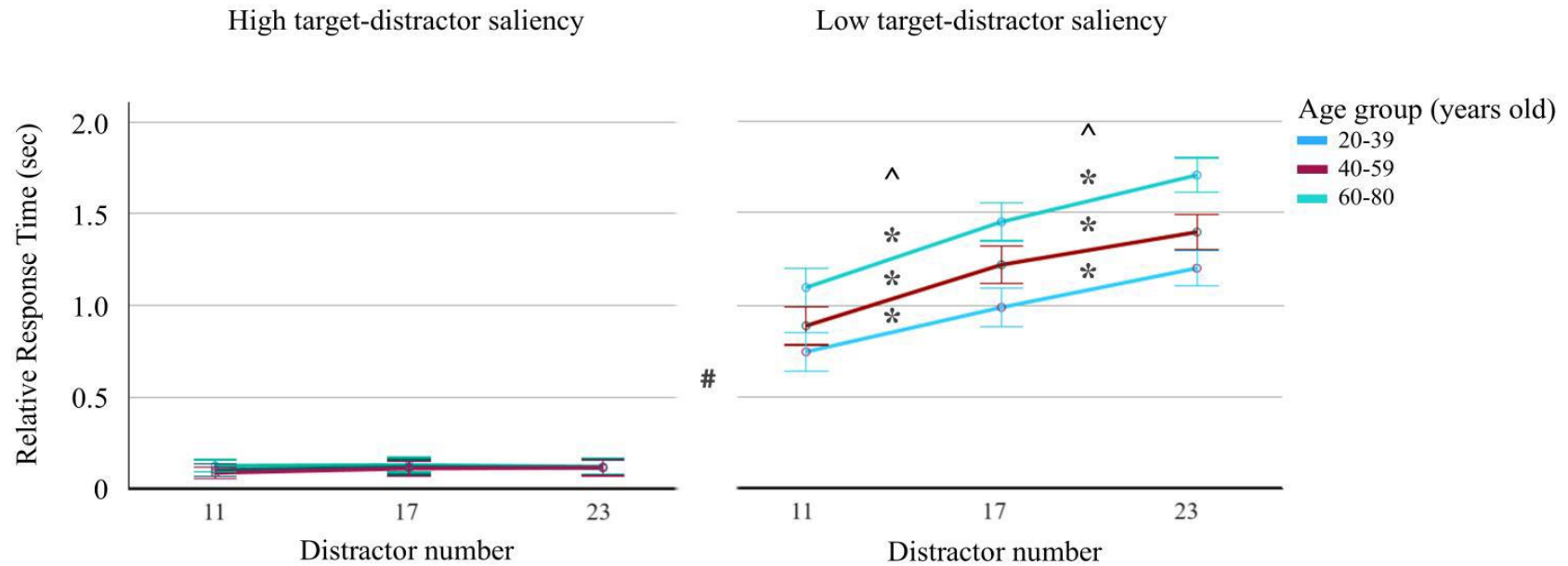


Figure 8. Mean RRT (seconds) for independent variables of target-distractor saliency, number of distractors and group. The left graph illustrates the high saliency condition, while the right graph shows the low saliency condition. Error bars represent 95% confidence intervals. Blue lines indicate participants aged 20-39 years, purple lines represent those aged 40-59 years, and green lines represent participants aged 60-80 years. Hash symbols ('#') indicate significant main effects of saliency; Carets ('^') indicate significant main effects of the number of distractors and Asterisks ('*') indicate significant main effects of age group. Results confirmed the

classic FIT pattern, with a significant increase in mean RRT as the number of distractors increased only under low saliency conditions. Additionally, a significant age effect was observed in the low saliency condition.

Chapter 4

ET outcomes

Statistical analyses on ET metrics were performed on a dataset of 12752 trials corresponding to the total dataset of levels with distractors minus 208 trials consisting of errors and omissions. No trials were excluded because of incorrect gaze starting position. We excluded 161 trials (1.26% of the initial dataset) that didn't end with a fixation of the target. The distractor fixation dataset was composed of 14489 measures.

Concerning the main ET outcomes (i.e., total cumulative time spent fixating on distractors and mean distractor fixation time), we then excluded 85 outliers (2.2%) for group 20-39 years, 104 outliers (2.1%) for group 40-59 years, and 112 outliers (1.9%) for group 60-80 years. The final dataset was thus composed of 14188 valid measures. Although the main analyses reported in the manuscript focused on fixation duration, for descriptive purposes we also provide, in the supplementary material, 3D plots of fixation counts across the playing field (Figure S2). These visualizations illustrate the relative distribution of attention across stimulus positions.

Total cumulative time spent fixating on distractors per trial

We found a significant main effect of (i) target-distractors saliency ($F(1, 42) = 219.581, p < 0.001, \eta^2 = 0.839$) and (ii) distractor number ($F(1, 42) = 150.102, p < 0.001, \eta^2 = 0.781$), with longer cumulative time spent fixating on distractors for low saliency condition and with increasing number of distractors (Figure 9).

The two-way interaction between target-distractors saliency and distractor number (FIT effect) was also significant ($F(2, 42) = 114.497, p < 0.001, \eta^2 = 0.732$). Post hoc analyses showed a significant main effect of distractor number in both (i) high saliency condition ($F(1, 42) = 26.050, p < 0.001, \eta^2 = 0.383$), and low saliency condition ($F(2, 42) = 135.864, p < 0.001, \eta^2 = 0.764$).

We also found a significant effect of group ($F(2, 42) = 3.231, p = 0.050, \eta^2 = 0.133$) with older age groups showing longer cumulative fixation times on distractors.

The interaction between target-distractor saliency and group was also significant ($F(2, 42) = 3.231, p = 0.050, \eta^2 = 0.133$). The effect of saliency was most pronounced in the group of 60-80 years, where the mean increased from $M = 0.031$ ($SD = 0.003$) in high saliency to $M = 0.342$ ($SD = 0.032$) in low saliency. A similar pattern was observed in group 40-59 years, with an increase from $M = 0.025$ ($SD = 0.003$) to $M = 0.280$ ($SD = 0.032$). In group 20-40 years, the effect was less marked, with means rising from $M = 0.022$ ($SD = 0.003$) to $M = 0.225$ ($SD = 0.032$).

The ANOVA for the high saliency condition showed a significant main effect of distractor number ($F(1, 42) = 26.050, p < 0.001, \eta^2 = 0.383$), with longer cumulative fixation times on distractors with increasing number of stimuli. For high saliency condition, the effect of group was not significant, ($F(2, 42) = 1.656, p = 0.203, \eta^2 = 0.073$).

The ANOVA for the low saliency condition showed a significant main effect of distractor number ($F(2, 42) = 135.864, p < 0.001, \eta^2 = 0.764$), with longer cumulative fixation times on distractors with increasing number of stimuli. A significant main effect of group ($F(2, 42) = 3.278, p = 0.048, \eta^2 = 0.135$) was also observed. For low target-distractor saliency, a significant main group effect was found between group 20-40 years and group 60-80 years ($F(1, 28) = 5.537, p = 0.026, \eta^2 = 0.165$), with older age groups showing longer cumulative fixation times on distractors. The other pairwise comparisons between groups did not reveal any statistically significant differences. (Figure 9, supplementary Table S2 lists the reference values for each condition).

Chapter 4

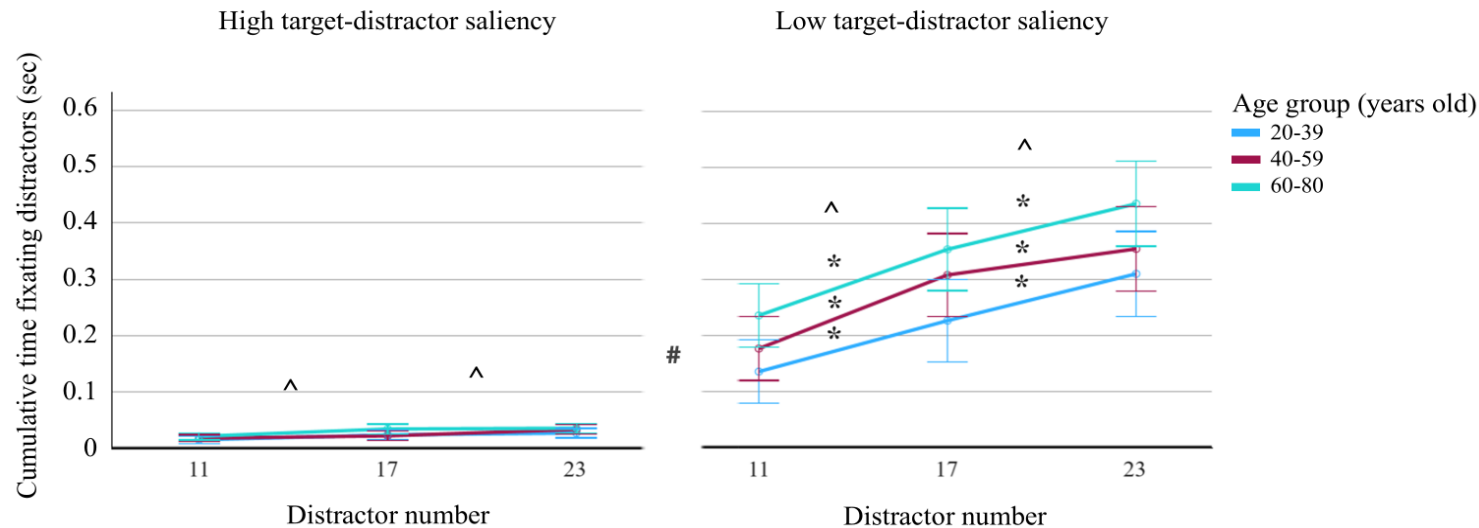


Figure 9. Total cumulative time spent fixating on distractors (seconds) for independent variables of target-distractor saliency, number of distractors and group. The left graph illustrates the high saliency condition, while the right graph shows the low saliency condition. Error bars represent 95% confidence intervals. Blue lines indicate participants aged 20-39 years, purple lines represent those aged 40-59 years, and green lines represent participants aged 60-80 years. Hash symbols ('#') indicate significant main effects of saliency; Carets ('^') indicate significant main effects of the number of distractors and Asterisks ('*') indicate significant main effects of age group. Results showed a significant main effect of target-distractors saliency, with longer cumulative fixation times in low saliency condition. A significant increase in mean cumulative fixation time was also observed as the number of distractors increased, for both high and low saliency conditions. Additionally, a significant age effect was observed in the low saliency condition.

Mean distractor fixation time

We did not find a significant main effect for target-distractors saliency ($F(1, 42) = 1.015$, $p = 0.320$, $\eta^2 = 0.024$), or distractor number ($F(1.738, 72.984) = 2.874$, $p = 0.070$, $\eta^2 = 0.064$). Similarly, there was no significant main effect of group ($F(2, 42) = 0.390$, $p = 0.679$, $\eta^2 = 0.018$).

None of the interactions reached significance, including the three-way interaction of saliency, distractor number, and group ($F(4, 84) = 0.798$, $p = 0.354$, $\eta^2 = 0.050$) (Figure 10, supplementary Table S3 lists the reference values for each condition).

Chapter 4

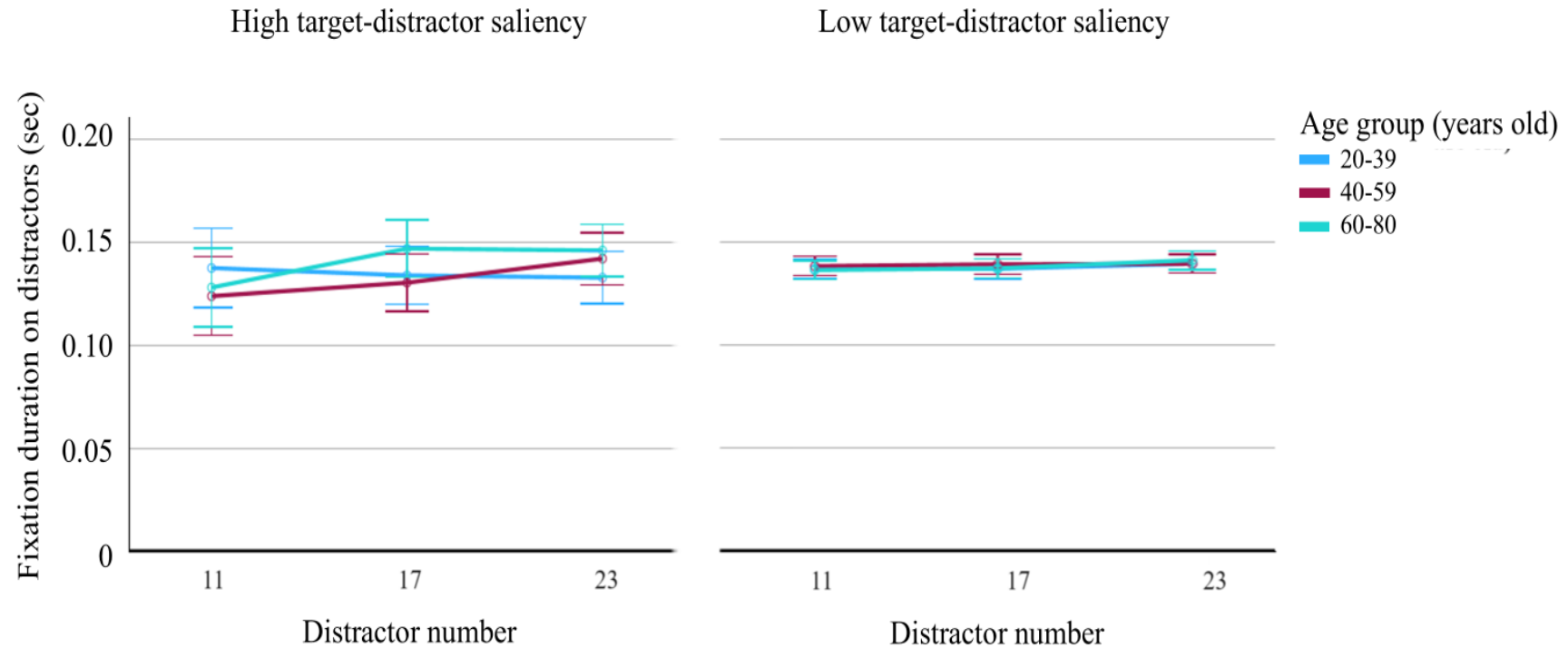


Figure 10. Mean fixation duration (seconds) for independent variables of target-distractor saliency, number of distractors and group. The left graph illustrates the high saliency condition, while the right graph shows the low saliency condition. Error bars represent 95% confidence intervals. Blue lines indicate participants aged 20-39 years, purple lines represent those aged 40-59 years, and green lines represent participants aged 60-80 years. No significant main effects or interaction were observed.

Distractor capture fixations

Concerning the distractor capture fixations number analysis, the total dataset was composed of 14216 measures. A three SD confidence interval filter was applied, removing 333 outliers. The analyses showed significant main effects for (i) target-distractors saliency ($F(1, 42) = 376.624, p < 0.001, \eta^2 = 0.900$) and (ii) distractor number ($F(1, 42) = 162.394, p < 0.001, \eta^2 = 0.795$). The interaction between saliency and distractor number was also significant ($F(1, 42) = 122.214, p < 0.001, \eta^2 = 0.744$). Separate ANOVAs for saliency showed a significant main effect of distractor number for both high ($F(2, 42) = 38.872, p < 0.001, \eta^2 = 0.481$) and low saliency conditions ($F(2, 42) = 145.793, p < 0.001, \eta^2 = 0.776$) (Figure 11, supplementary Table S4 lists the reference values for each condition), with increasing number of capture fixations on distractors with increasing number of stimuli. For the between-subjects effects, the main effect of group was not significant ($F(2, 42) = 2.032, p = 0.144, \eta^2 = 0.088$) and there were no significant interactions with group.

Chapter 4

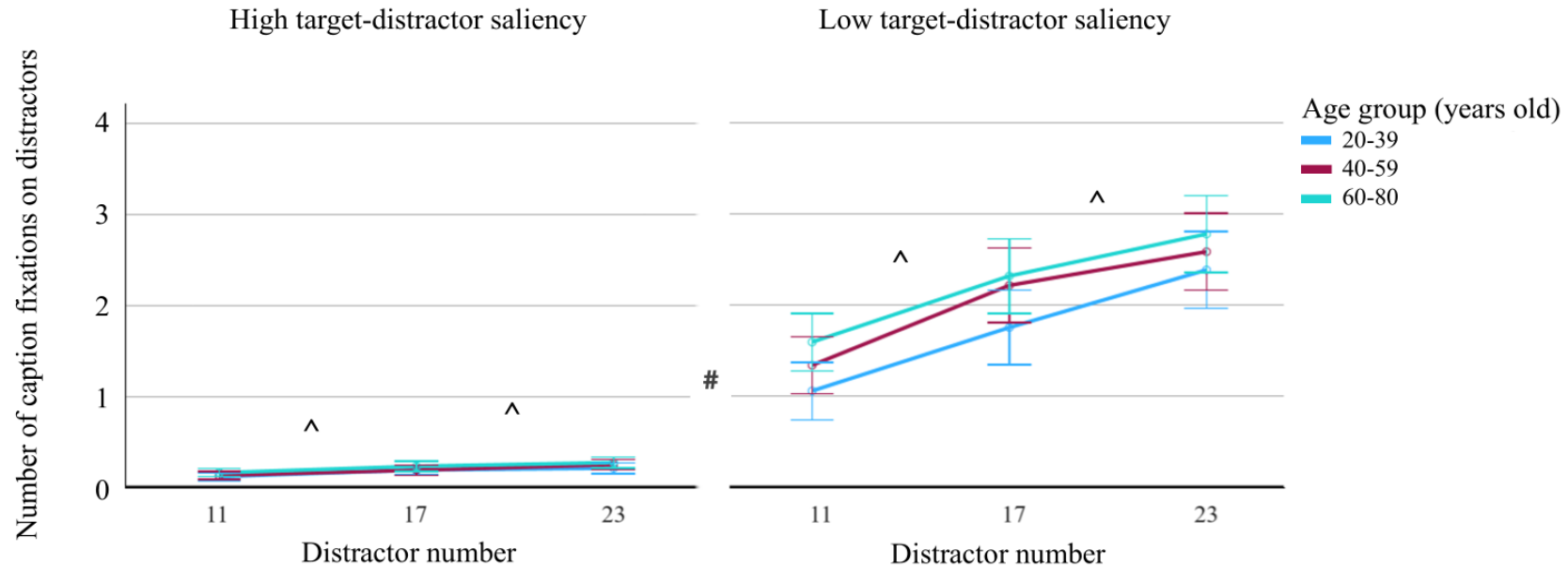


Figure 11. Mean number of caption fixations on distractors for independent variables of target-distractor saliency, number of distractors and group. The left graph illustrates the high saliency condition, while the right graph shows the low saliency condition. Error bars represent 95% confidence intervals. Blue lines indicate participants aged 20-39 years, purple lines represent those aged 40-59 years, and green lines represent participants aged 60-80 years. Hash symbols ('#') indicate significant main effects of saliency; Carets ('^') indicate significant main effects of the number of distractors and Asterisks ('*') indicate significant main effects of age group. Results showed a significant main effect of target-distractors saliency, with higher number of capture

fixations in low saliency condition. A significant increase in mean number of capture fixations as the number of distractors increased was also observed for both high and low saliency conditions. No age effect was observed.

Chapter 4

Distractor re-capture fixations

Concerning the distractor re-capture fixations number analysis, the total dataset was composed of 614 measures. A three SD confidence interval filter was applied, removing 3 outliers from group 60-80 years.

We found a significant main effect for (i) target-distractors saliency ($F(1,42) = 57.307$, $p < 0.001$, $\eta^2 = 0.577$) and (ii) distractor number ($F(1,42) = 27.634$, $p < 0.001$, $\eta^2 = 0.397$).

The interaction between saliency and distractor number was also significant ($F(1, 42) = 27.925$, $p < 0.001$, $\eta^2 = 0.399$). Posthoc analyses showed that the ANOVA for the high saliency condition showed no significant main effect of distractor number ($F(2,42) = 1.000$, $p = 0.372$, $\eta^2 = 0.023$), whereas the ANOVA for the low saliency condition showed a significant main effect of distractor number ($F(2, 42) = 27.845$, $p < 0.001$, $\eta^2 = 0.399$), with increasing number of re-capture fixations on distractors with increasing number of stimuli.

A significant main effect of group ($F(2,42) = 5.256$, $p = 0.009$, $\eta^2 = 0.200$) was found. However, the interaction between distractor number and group was not significant, ($F(4, 42) = 1.231$, $p = 0.306$, $\eta^2 = 0.055$) (Figure 12, supplementary Table S5 lists the reference values for each condition).

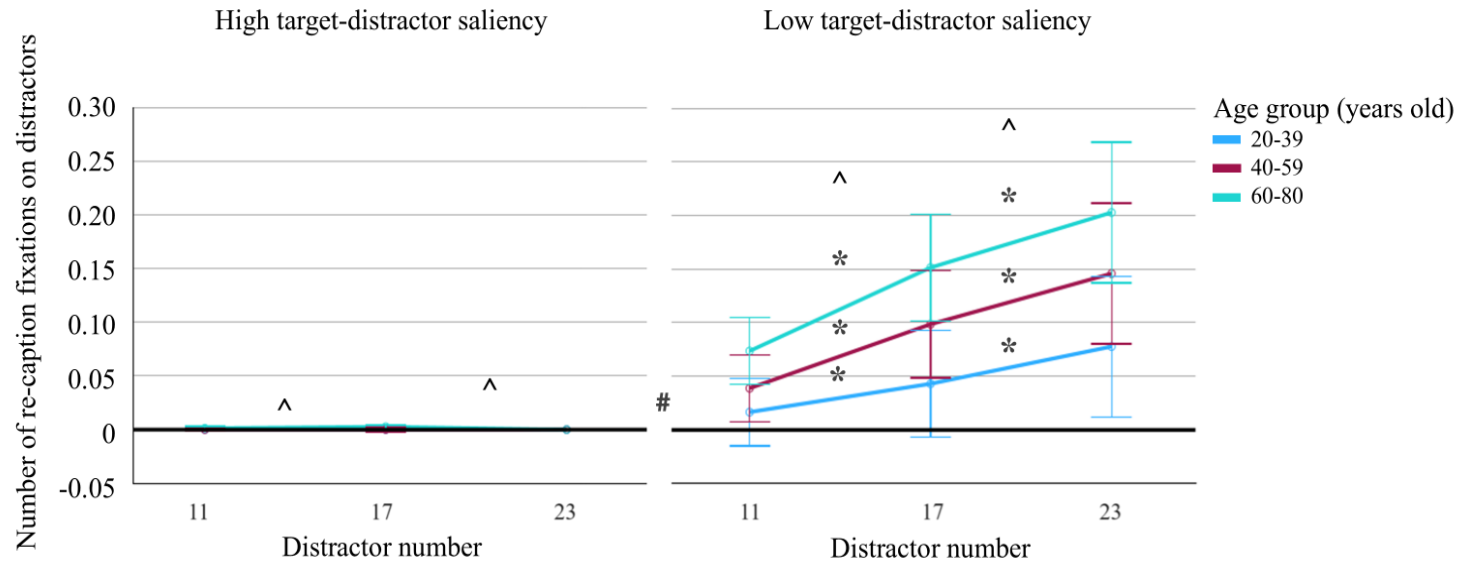


Figure 12. Mean number of re-capture fixations on distractors for independent variables of target-distractor saliency, number of distractors and group. The left graph illustrates the high saliency condition, while the right graph shows the low saliency condition. Error bars represent 95% confidence intervals. Blue lines indicate participants aged 20-39 years, purple lines represent those aged 40-59 years, and green lines represent participants aged 60-80 years. Hash symbols ('#') indicate significant main effects of saliency; Carets ('^') indicate significant main effects of the number of distractors and Asterisks ('*') indicate significant main effects of age group. Results showed a significant main effect of target-distractors saliency, with higher number of re-capture fixations in low saliency condition. A significant increase in mean number of re-capture fixations was also

Chapter 4

observed as the number of distractors increased, for both high and low saliency conditions. Additionally, a significant age effect was observed in the low saliency condition.

Kinematic outcomes

As for ET metrics, statistical analyses on kinematic metrics were performed on a dataset of 12,752 trials. A three SD confidence interval filter was applied to each variable. After filtering, the number of valid trials per metric was as follows: Mean Velocity (12,648 trials), Peak Velocity (12,571 trials), SPARC (12,390 trials), and Coefficient of Variation of Velocity (12,501 trials).

Mean Velocity

We found a significant main effect for (i) response hand ($F(1,42) = 5.320$, $p = 0.026$, $\eta^2 = 0.112$) and (ii) group ($F(2,42) = 20.488$, $p < 0.001$, $\eta^2 = 0.494$). The interaction between group and response hand was not significant ($F(2,42) = 0.559$, $p = 0.576$, $\eta^2 = 0.026$). The significant main group effect showed differences between: (i) group 20-39 years and group 40-59 years ($F(1, 28) = 17.591$, $p < 0.001$, $\eta^2 = 0.386$), (ii) group 40-59 years and group 60-80 years ($F(1, 28) = 5.746$, $p = 0.023$, $\eta^2 = 0.170$) and (iii) group 20-40 years and group 60-80 years ($F(1, 28) = 41.797$, $p < 0.001$, $\eta^2 = 0.599$), with a gradual reduction in mean velocity as the group's mean age rises (supplementary Table S6.a.b list the reference values for group and response hand).

Peak Velocity

A significant group effect ($F(2,42) = 9.733$, $p < 0.001$, $\eta^2 = 0.317$) was observed, but no response hand effect ($F(1,42) = 3.156$, $p = 0.083$, $\eta^2 = 0.070$) and no interaction between group and response hand ($F(2,42) = 0.876$, $p = 0.424$, $\eta^2 = 0.040$). The significant main group effect showed differences between: (i) group 40-59 years and group 60-80 years ($F(1, 28) = 6.046$, $p = 0.020$, $\eta^2 = 0.178$) and (ii) group 20-39 years and group 60-80 years ($F(1, 28) = 20.721$, $p < 0.001$, $\eta^2 = 0.425$), with a gradual reduction in peak velocity as the group's mean age rises (supplementary Table S7).

Chapter 4

SPARC

Group ($F(2,42) = 0.917$, $p = 0.407$, $\eta^2 = 0.042$) and response hand ($F(2,42) = 0.025$, $p = 0.876$, $\eta^2 = 0.001$) effects were not significant. The interaction between group and response hand was also not significant ($F(2,42) = 1.911$, $p = 0.161$, $\eta^2 = 0.083$).

Coefficient of variation of the velocity

Group ($F(2,42) = 0.413$, $p = 0.664$, $\eta^2 = 0.019$) and response hand ($F(2,42) = 0.030$, $p = 0.862$, $\eta^2 = 0.001$) effect were not significant. The interaction between group and response hand was also not significant ($F(2,42) = 0.101$, $p = 0.905$, $\eta^2 = 0.005$).

Discussion

This study aimed to present REAsmash-ET, a methodological framework for the integrated assessment of visuospatial attention and UL motor control in iVR. Through the combination of behavioral outcomes, ET metrics and kinematic analysis within a structured search-and-reach task, we tested three main hypotheses. First, based on FIT, we hypothesized that behavioral outcomes, specifically RTs, would vary as a function of target-distractor saliency, number of distractors. Second, we hypothesized that eye-tracking metrics would reflect differences in visual search strategies under different task conditions. Third, we hypothesized that kinematic metrics would capture variations in motor performance associated with hand dominance, providing complementary information on UL function. We also hypothesized an age effect on RT, ET metrics and motor control.

The behavioral outcomes confirmed the reliability of our SG in replicating the FIT in a different HMD set-up relative to previous studies with REAsmash^{124,132,220}. We observed progressively longer RTs as the number of distractors increased, but only in the low salience target-distractor condition. This effect was accompanied by a clear age-related decline in RRT specifically for the low salience target-distractor condition. Consistent with previous studies employing REAsmash on healthy

participants^{132,219,220}, the frequency of errors and omissions remained very low, confirming the reliability of the task.

Overall, ET metrics confirm the REAsmash-ET as an effective framework for measuring the cognitive cost of visual search under different stimuli conditions and assessing visual exploration strategies. In accordance with the FIT, the total fixation time spent on distractors showed a significant interaction between target-distractor salience and the number of distractors, with progressively higher values when the number of distractors increased for the low salience condition. While statistical significance for distractor number was observed for some ET dependent variables in high salience conditions, these effects were much smaller than the effects in the low salience conditions (see the accompanying figures and tables in the supplementary material), and likely clinically irrelevant. In the high salience conditions, the time spent looking at distractors remained close to zero regardless of the distractor number. This finding confirms that participants detected the target with minimal engagement of distractors, likely relying on bottom-up processes typical of parallel search^{37,211}.

In low-salience conditions, consistent with top-down processing involved in visual serial search^{37,211}, the effect of distractor number was both robust and clinically relevant. In this low saliency condition, compared to the 11-distractor level, the mean total cumulative time spent fixating on distractors increased by 62% and 100% with 17 and 23 distractors respectively.

The emergence of group differences further supports the ability of REAsmash-ET in detecting subtle variations in visual attention performance across the lifespan, even in a healthy population. This is consistent with previous evidence showing that ageing is associated with reduced visual search efficiency, particularly in tasks requiring serial attentional processes, with older adults exhibiting slower response times and altered gaze patterns when confronted with increased visual complexity²⁵².

Regarding the mean duration of distractor fixations, no significant effects were found for target-distractor saliency, distractor number, or age group,

Chapter 4

nor were any interactions observed. Results on distractor fixation duration suggest that, while task complexity influences how often participants fixate on distractors, the length of each fixation remains substantially stable, regardless of search difficulty or age in healthy individuals. As suggested by previous research^{253,254}, under conditions of time pressure, as in the REAsmash-ET, fixation durations may remain stable regardless the stimuli set (i.e., features and number of distractors), likely due to limited time for attentional adjustment. This feature of REAsmash-ET is expected to provide a valuable framework for future comparisons between individuals with cognitive impairments and normative data from healthy controls. The present findings allow us to speculate that in the presence of cognitive impairments, individuals may exhibit longer average fixation durations. This may indicate a reduced ability to adapt to the temporal constraints of the task, which requires exploring as many stimuli as possible within a limited time window, while maintaining an organized search path and ensuring sufficient accuracy in distractor detection and inhibition.

While disruptive effect of distractors on performance is well established, with numerous replications in the literature^{39,41}, yet no tool for assessing distractor inhibition is available in routine clinical practice. From a clinical standpoint, prolonged fixations on distractors may serve as a marker of impaired distractor inhibitory control, which in patients could manifest as slowed information processing and greater susceptibility to interference in everyday tasks. REAsmash-ET ability to elicit and assess distractor inhibitory control is thus particularly valuable in stroke survivors, where deficits in attentional control can hinder functional recovery and daily performance²⁵⁵.

Building on these considerations, we analyzed the results related to overlapping fixations with a focus on serial search. These metrics allowed us to further investigate whether and how REAsmash-ET can detect the efficiency of visual exploration from a spatial perspective (i.e., spatial distribution of a sequence of fixations). Concerning capture fixations, our results suggest that the likelihood of consecutive fixations on the same distractor increases with the number of distractors on the playing field,

regardless of the age of the participant. According to the literature, a pathological number of capture fixations likely indicates difficulties with attentional disengagement^{211,246,248}. However, our data suggests that during complex search tasks, capture fixations are present even in healthy controls. This consideration calls for the introduction of normative data if the aim is to introduce these metrics in cognitive assessment.

Although re-capture events were extremely rare, significant age-related differences emerged, particularly between younger and older participants. These differences reflect subtle variations in spatial exploration efficiency, highlighting the capacity of REAsmash-ET in detecting age-related changes in attentional control, reinforcing its value beyond clinical diagnostics. These results support the proposed methodological approach and confirm its potential for use in both normative research and clinical adaptation for assessing visual attention in naturalistic goal-directed immersive settings.

Overlapping fixation patterns mirror clinical profiles commonly observed in patients with right hemisphere stroke²⁵⁶ or frontal executive dysfunction²⁵⁷. Clinically, excessive capture or re-capture fixations may signal inefficient allocation of (inhibitory) attentional resources and working memory, linked to disorganized visual exploration after stroke. An increase in capture fixations indicates difficulty disengaging from irrelevant stimuli, reflecting impaired distractor inhibition. Increased re-capture fixations (i.e., perseveration)^{211,246,248} is caused by a combination of visuospatial working memory and the inability to correctly inhibit a previously viewed distractor^{209,246,247}. These findings highlight the potential of REAsmash-ET for fine-grained diagnostic assessment.

Concerning UL speed metrics, findings align with previous works with REAsmash⁹⁹, showing that both mean and peak velocity slow with age. As expected, the dominant UL was faster than the non-dominant one, confirming the ability of REAsmash to detect asymmetries in motor performance even within healthy participants. However, the lack of significant interaction between age and response hand suggests that age-related slowing occurs equally in both ULs. Movement smoothness,

Chapter 4

measured by SPARC, was not significantly affected by age or response hand, indicating that older adults maintain relative smooth trajectories despite moving more slowly. Similarly, movement consistency, assessed through the coefficient of variation of velocity, remained stable across age groups and response hand. These findings highlight the value of REAsmash-ET in detecting age-related motor changes while distinguishing between declines in movement speed and the preservation of movement quality. The stability of smoothness and consistency is particularly relevant, as their deterioration is typically associated with pathological motor impairment rather than healthy ageing. These results may serve as an initial reference point for exploring motor performance in clinical populations, particularly in conditions characterized by unilateral motor deficits. Beyond statistical differences across age groups, these kinematic measures provide clinically relevant insights into motor efficiency. By revealing diminished motor control in older participants, reductions in peak velocity highlight the capacity of these measures to discriminate within the healthy spectrum, thereby underscoring their value for probing pathological motor deficits, as documented in post-stroke populations^{178,258,259}. Importantly, these continuous, objective measures should overcome the floor and ceiling effects of traditional ordinal scales, supporting the development of more precise and individualized assessments of motor recovery complementary to conventional clinical assessments.

Unlike previous iVR-ET studies, which have predominantly focused on passive or non-motor visual exploration tasks, REAsmash-ET combines active motor responses with structured visual search, allowing the simultaneous investigation of attentional and motor dynamics within a single naturalistic goal-directed immersive framework²⁶⁰. By interpreting the results within this clinical framework, REAsmash-ET emerges not only as a methodological innovation but also as a tool that can contribute to advancing neurorehabilitation practice by supporting the integrated assessment of cognitive and motor functions within a single task.

Limitations

The present study aimed to define a framework for the extraction and interpretation of eye-tracking metrics in a structured search-and-reach task. As a preliminary investigation of the reliability of a novel methodological approach, we acknowledge that the present study has several limitations. Because only healthy participants were included, the present study does not allow us to draw conclusions regarding the ability of REAsmash-ET to detect motor deficits or to capture cognitive-motor interference effects that typically occur in clinical populations, such as stroke. The next step will be to test REAsmash-ET in a post-stroke population, where aspects such as consistency, sensitivity, reliability, and convergent validity with established gold-standard assessments will be systematically addressed. Preliminary results also suggest a potential age-related effect even among healthy individuals, particularly in visual search patterns such as re-capture fixations. However, the sample size of the present study was not designed to establish normative data, and these findings are therefore not conclusive. Future studies will include larger samples to further investigate the effect of age on overlapping fixations.

Although participant groups were balanced for gender, no statistical analyses were conducted to investigate gender-related effects. This choice was based on previous findings and theoretical frameworks, such as the FIT, which suggest that cognitive and attentional processes involved in the primary task are unlikely to be influenced by gender¹²⁵. Therefore, gender was not considered a critical factor for the current research aims. Nevertheless, we acknowledge that gender may still play a role in other dimensions, such as technology use or task engagement, and future studies should consider exploring these aspects more specifically.

Recent work with REAsmash has shown that HMD hand controllers can provide reliable and sensitive kinematic measures to capture training-related changes in motor learning²⁶¹. However, it remains a limitation that VR-based kinematics are not fully equivalent to real-world movements, as the use of such controllers may influence natural motor execution. The absence

Chapter 4

of physical object interaction and reduced haptic feedback can subtly affect movement trajectories, especially during the deceleration and endpoint phases²⁶².

Implications and Perspectives

We consider REAsmash-ET a task of functional relevance, as it engages naturalistic goal-directed visuomotor behavior under standardized conditions. REAsmash-ET offers a robust and flexible framework for studying the interplay between cognitive and motor processes in immersive VR contexts. By combining behavioral, eye-tracking and UL kinematic data within structured task manipulations, it enables a multidimensional investigation of visual search, attentional control, and motor execution. This makes it a valuable tool for fundamental research on how attention and action co-regulate under time and performance constraints.

From a clinical perspective, REAsmash-ET holds strong potential for assessing the interaction between cognitive functions frequently impaired in stroke survivors. For example, its metrics on distractor engagement and fixation dynamics may support the identification of attentional disengagement difficulties, such as those observed in USN²⁴⁸. Moreover, the framework could help explore how spatial working memory and selective attention interact during visual exploration, offering insights into compensatory mechanisms or deficits in goal-directed behavior. By highlighting individual profiles of cognitive-motor interplay, REAsmash-ET may inform targeted assessments and personalized rehabilitation strategies in clinical populations.

As a planned extension of the REAsmash-ET framework, we aim to further investigate the interplay between cognitive and motor processes by segmenting upper limb kinematic data into distinct phases relative to eye-tracking events. Specifically, we will distinguish (i) a first scanning phase, during which stimuli are displayed on the field but the target has not yet been fixated; (ii) a second phase, starting from the first fixation of the target and extending to the manual response / the end of the trial. By contrasting

post-stroke patients with healthy controls, this approach will allow us to explore in greater detail how cognitive demands and motor execution interact across task stages, thereby providing a more precise characterization of cognitive-motor interference under dual-task conditions. Furthermore, future analyses will leverage the recorded head coordinates to disentangle the relative contributions of head and eye movements to gaze deployment in REAsmash-ET.

While this study was limited to healthy participants, the results support the potential clinical utility of REAsmash-ET as a single-task framework integrating information that currently requires multiple assessment tools. For instance, visuospatial attention is typically evaluated through subtests of the TAP battery¹³¹, while upper limb function is assessed with scales such as the Fugl-Meyer Assessment¹⁶³. REAsmash-ET offers the possibility to capture both domains simultaneously and, importantly, provides metrics on distractor inhibition, a cognitive ability for which no standardized clinical test is currently available. This integrated approach could therefore streamline assessment protocols, while future studies in clinical cohorts will be needed to confirm its applicability and diagnostic value.

An additional advantage of REAsmash-ET is its ease of use, which minimizes the learning curve for clinical personnel and facilitates rapid implementation in rehabilitation settings. Unlike classical non-immersive systems, which would require the parallel use of external eye-tracking devices and additional kinematic sensors to obtain the same range of information, REAsmash-ET provides an integrated solution that captures behavioral, oculomotor, and kinematic data with a single device.

In addition, we are currently developing a fully adaptive algorithm in which AD tolerance is continuously adjusted to the average distance between eyes and consecutive gaze points. This approach is designed to keep LD constant within a physiologically meaningful AD range and to account for individual differences (e.g., height, posture), thereby supporting more robust and individualized fixation detection in future implementations of REAsmash-ET.

Chapter 4

Beyond its application in post-stroke assessment, our main target population, the REAsmash-ET framework may also have utility in other neurological conditions, such as mild cognitive impairment and early-stage dementia, where deficits in distractor inhibition, spatial and non-spatial attention have often been reported²⁶³. Its multidimensional approach could contribute to the early identification and characterization of attentional and working memory dysfunctions across clinical populations.

In terms of ET algorithm, our semi-adaptive approach aims to provide a generalizable solution for fixation detection in immersive 3D environments, by adapting the angular dispersion threshold based on the average eye-to-stimulus distance. Unlike purely spatial (Euclidean) methods that require precise 3D gaze coordinates, this method can be applied in situations where such data are unavailable, as long as an approximate stimulus distance is known or can be assumed.

Conclusions

This study introduced REAsmash-ET, a novel and generalizable methodological framework for combined cognitive and motor assessment in iVR. By combining behavioral outcomes, ET and UL kinematic measures within a naturalistic goal-directed search-and-reach task, REAsmash-ET enables the simultaneous investigation of attentional and motor control and their interaction.

The framework's structure, data processing pipeline, and convergence with theoretical predictions from FIT support its robustness and feasibility for future applications.

Beyond its current implementation, REAsmash-ET is designed to be flexible and scalable, making it suitable for adaptation to other tasks, patient groups, or rehabilitation contexts. Taken together, these findings highlight the value of a multidimensional, theory-driven approach for advancing research and clinical assessment of motor-cognitive interactions in both healthy and neurological populations.

Declarations

Ethics approval and consent to participate

The protocol was approved by the Saint Luc-UCL Hospital-Faculty Ethics Committee (Belgium) (2015/10FEV/053) prior to the initiation of the study and registered on clinicaltrials.gov (NCT04694833).

Availability of data and materials

The datasets used during the current study are openly available in the open data archive of University of Louvain (<https://dataverse.uclouvain.be/dataset.xhtml?persistentId=doi:10.14428/DVN/GWVH3W>).

Competing interests

The authors declare that they have no competing interests. Funding The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

Authors' contributions

GS designed the presented study, analyzed the data, interpreted the results and wrote the paper. GE, TL and MGE created the REAsmash, interpreted the results of the present paper, and helped write the paper. MM and NB interpreted the results of the present paper and helped write the paper. All authors contributed to editorial revisions in the manuscript. All authors read and approved the final manuscript. All authors have participated actively in the work and accepted responsibility for all aspects of the work.

Acknowledgements

We thank Stephane Grade, Fabrice Gerard and Clement Letesson for providing help and support with the REAsmash-ET software development.

Chapter 4

Supplementary Information

The online version includes supplementary material containing (i) reference values for ET metrics and UL kinematics extracted from our study population; (ii) a graphical representation of the spatial distribution of distractor fixations across the playing field in the three age groups; (iii) the experimental setting and visual angles and (iv) a technical note concerning the instrument-level calibration and software validation tests for eye tracking and upper-limb tracking.

Supplementary Material

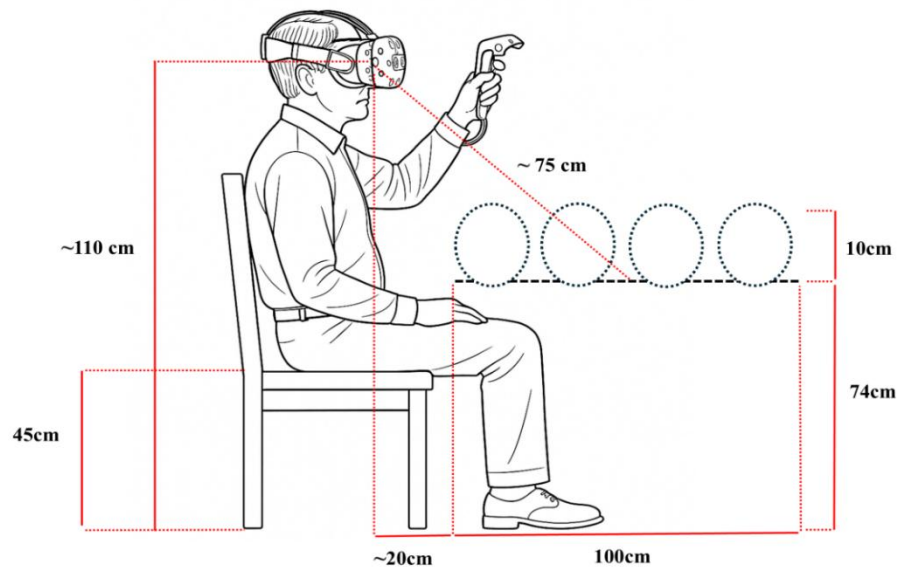


Figure S1. Side-view illustration of the experimental setting. The red lines indicate real-world dimensions: eye height ~110 cm, seat height 45 cm, table height 74 cm, table depth 100 cm, and an eye-to-playing-surface center distance of ~75 cm (the head is ~70 cm behind and 35 cm above the table center). The virtual objects (i.e., the playing surface and the stimuli) are schematically represented with dotted black lines, with ROI helmet centers ~10 cm above the playing field.

Relative to the participant's seated resting posture depicted in the figure, the playing field had a visual angle of ~120° horizontally and ~40° vertically. The 3D space covered by the stimuli had maximum angles of ~115° horizontally and ~35° vertically.

The following table (Table S1) reports, for each row of stimuli on the playing surface, the mean edge-to-edge angular gap between adjacent stimuli and the within-row range. The overall mean angular gap across all rows was ~ 8°.

Chapter 4

Table S1. Edge-to-edge angular gap between adjacent stimuli.

Row	Mean gap (°)	Range within row (°)
Row 1 (proximal)	11.40	5.42 - 21.37
Row 2 (intermediate proximal)	8.60	6.22 - 11.54
Row 3 (intermediate distal)	6.70	5.64 - 7.89
Row 4 (distal)	5.41	4.87 - 5.99

These data illustrate the relative frequency with which different areas of the playing field were explored. Across all groups, fixations were not uniformly distributed but rather showed higher concentration in central columns. Contrasts between age groups showed an age-related increase in overall fixation counts. A left-right asymmetry emerged, with a predominance of fixations on the left relative to right side of the field. This pattern may reflect population bias, as all participants belonged to Western cultures where visual exploration typically follows a left-to-right scanning strategy, consistent with reading habits^{264–266}.

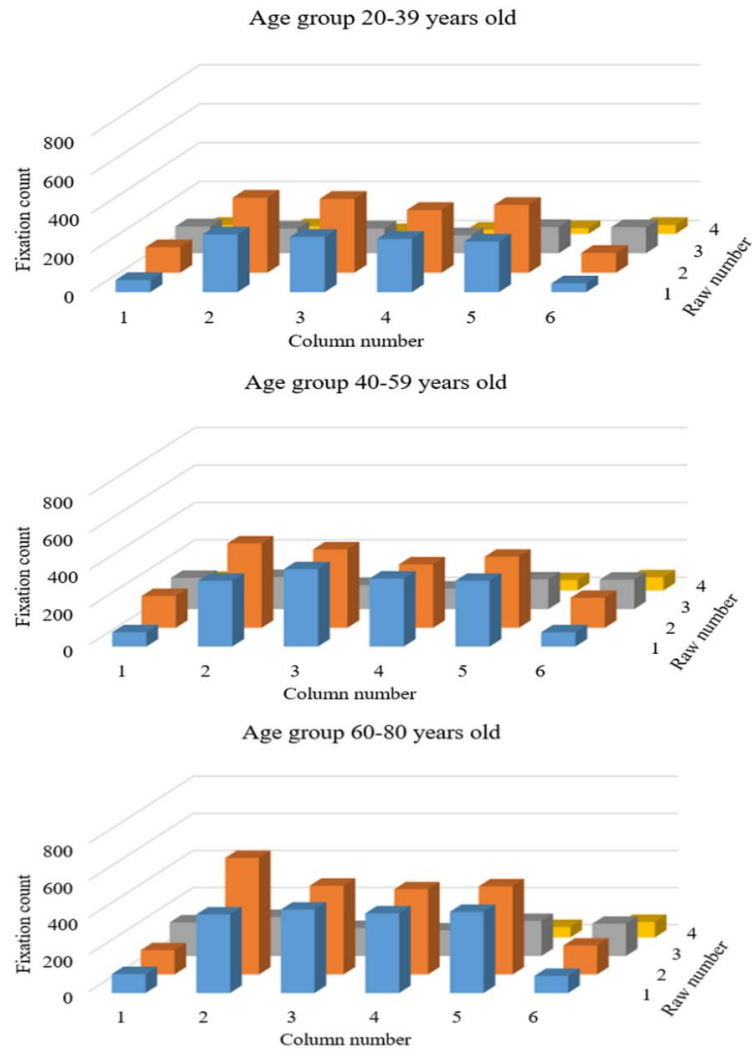


Figure S2. Spatial distribution of distractor fixations across the playing field in the three age groups. The 3D bar plots presents the total number of valid fixations (after 3 SD outlier removal) for each stimulus position on the 6×4 playing surface. The three plots are for the 20-39, 40-59, and 60-80 years-old groups. Bars indicate total fixation number per distractor locations, all trials merged (x-axis = column position; z-axis = row position; y-axis = fixation count).

Chapter 4

Table S2. Reference values for total cumulative time (seconds) spent fixating on distractors according to age group, target-distractor saliency and distractor number.

Age Group	Target-Distractor Saliency	Distractor Number	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
20-39	High	11	0,016	0,003	0,009	0,022
		17	0,024	0,004	0,016	0,033
		23	0,028	0,004	0,019	0,036
	Low	11	0,136	0,028	0,08	0,193
		17	0,227	0,036	0,153	0,3
		23	0,31	0,037	0,235	0,386
40-58	High	11	0,018	0,003	0,012	0,025
		17	0,023	0,004	0,014	0,031
		23	0,034	0,004	0,026	0,042
	Low	11	0,177	0,028	0,121	0,234
		17	0,308	0,036	0,235	0,382
		23	0,355	0,037	0,279	0,43
60-80	High	11	0,022	0,003	0,015	0,028
		17	0,035	0,004	0,026	0,043
		23	0,036	0,004	0,028	0,044
	Low	11	0,236	0,028	0,18	0,293
		17	0,354	0,036	0,28	0,427
		23	0,435	0,037	0,359	0,511

Table S3. Reference values for mean duration (seconds) for distractor fixation according to age group, target-distractor saliency and distractor number.

Age Group	Target-Distractor Saliency	Distractor Number	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
20-39	High	11	0,137	0,009	0,118	0,156
		17	0,134	0,007	0,12	0,148
		23	0,133	0,006	0,12	0,145
	Low	11	0,137	0,002	0,132	0,141
		17	0,137	0,002	0,132	0,142
		23	0,139	0,002	0,135	0,144
40-58	High	11	0,124	0,009	0,105	0,143
		17	0,13	0,007	0,116	0,144
		23	0,142	0,006	0,129	0,154
	Low	11	0,138	0,002	0,133	0,143
		17	0,139	0,002	0,134	0,144
		23	0,139	0,002	0,135	0,144
60-80	High	11	0,128	0,009	0,109	0,147
		17	0,147	0,007	0,133	0,161
		23	0,146	0,006	0,133	0,158
	Low	11	0,136	0,002	0,132	0,141
		17	0,137	0,002	0,132	0,142
		23	0,141	0,002	0,136	0,146

Chapter 4

Table S4. Reference values for distractor capture fixation number according to age group, target-distractor saliency and distractor number.

Age Group	Target-Distractor Saliency	Distractor Number	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
20-39	High	11	0,119	0,021	0,077	0,162
		17	0,193	0,027	0,139	0,247
		23	0,213	0,029	0,154	0,271
	Low	11	1,051	0,156	0,737	1,366
		17	1,747	0,203	1,337	2,157
		23	2,379	0,21	1,955	2,803
40-58	High	11	0,133	0,021	0,091	0,176
		17	0,192	0,027	0,137	0,246
		23	0,251	0,029	0,193	0,31
	Low	11	1,333	0,156	1,019	1,648
		17	2,21	0,203	1,8	2,619
		23	2,579	0,21	2,155	3,003
60-80	High	11	0,163	0,021	0,12	0,205
		17	0,233	0,027	0,179	0,288
		23	0,274	0,029	0,215	0,332
	Low	11	1,588	0,156	1,273	1,902
		17	2,313	0,203	1,903	2,722
		23	2,774	0,21	2,35	3,197

Table S5. Reference values for distractor re-capture fixation number according to age group, target-distractor saliency and distractor number.

Age Group	Target-Distractor Saliency	Distractor Number	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
20-39	High	11	0	0,001	-0,002	0,002
		17	0	0,001	-0,002	0,002
		23	0	0	0	0
	Low	11	0,017	0,016	-0,015	0,048
		17	0,043	0,025	-0,007	0,093
		23	0,078	0,032	0,012	0,143
40-58	High	11	0	0,001	-0,002	0,002
		17	0	0,001	-0,002	0,002
		23	0	0	0	0
	Low	11	0,039	0,016	0,008	0,07
		17	0,099	0,025	0,049	0,149
		23	0,146	0,032	0,08	0,211
60-80	High	11	0,001	0,001	0	0,003
		17	0,003	0,001	0,001	0,005
		23	0	0	0	0
	Low	11	0,074	0,016	0,042	0,105
		17	0,151	0,025	0,101	0,201
		23	0,203	0,032	0,137	0,268

Chapter 4

Table S6. Reference values for group (a.) and response hand for mean velocity (m/sec).

a.

Age Group	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
20-39	0,579	0,017	0,544	0,613
40-59	0,514	0,017	0,479	0,548
60-80	0,425	0,017	0,39	0,459

b.

Response Hand	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Dominant	0,513	0,011	0,491	0,536
Non-dominant	0,498	0,01	0,478	0,518

Table S7. Reference values for peak velocity (m/sec) according to age group.

Age Group	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
20-39	1,978	0,074	1,828	2,128
40-59	1,72	0,074	1,57	1,87
60-80	1,515	0,074	1,364	1,665

Technical note

Instrument-level calibration and validation tests for eye tracking and upper-limb tracking

In response to the reviewer's concern that the manuscript did not report instrument-level calibration or accuracy checks for eye tracking (ET) and upper-limb (UL) tracking and that behavioral consistency alone is insufficient, this technical note documents the tests we performed to verify measurement accuracy, precision, and stability.

Beyond the reported Methods, we implemented and verified the ET pipeline at software and data levels. The calibration criteria used to configure the fixation parser (i.e., number of fixations, percentage of points in fixation, mean fixation duration, and percentage of fixations within the region of interest, ROI) were implemented and unit-tested to ensure functional correctness. We replicated the calibration plots across ranges of dispersion and duration values to check expected monotonic patterns and to confirm that conclusions were stable within a reasonable neighborhood of parameters (Figure 1).

At the component level, the identification-by-dispersion-threshold (I-DT) algorithm was exercised on controlled cases: temporal-window construction, sampling-frequency checks, gaze-vector and dispersion-angle computation, and edge conditions (e.g., missing samples, boundary crossings). The Unity implementation was then cross-checked against a reference implementation¹. Discrepancies exposed defects in the published version which, once corrected, yielded matching outputs between both versions.

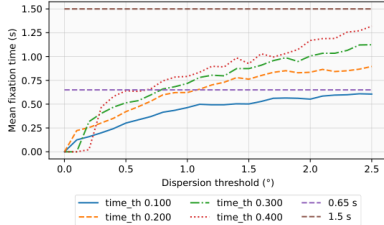
In the post-processing stage, we verified the reaction-time script through integration tests that cross-checked, for each trial, the fixation timestamps (before and after target selection) against the recorded reaction times, to ensure temporal alignment between gaze and behavioral data. We also performed directory and output structure tests to confirm that the script consistently located the correct input files and produced reproducible output

Chapter 4

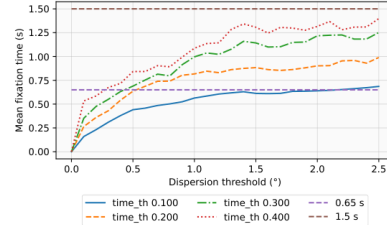
files with a stable naming and schema across all participants. We also ran researcher user testing to verify that installation and execution procedures were robust for non-developer use. During runtime profiling, we identified a software-development-kit (SDK) callback interaction that degraded performance and adjusted the data-collection flow to avoid contention, restoring stable acquisition (Figure 2).

For UL signals, operational quality control focused on pose availability (proportion of frames with valid six-degrees-of-freedom, 6-DOF, controller pose) and simple geometric sanity checks on instructed straight segments (straightness ratio and mean orthogonal deviation to a best-fit line), with unstable segments flagged for review/exclusion.

Mean Fixation Time Plots

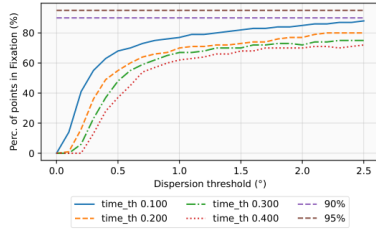


(a) Mean fixation time with the corrected I-DT algorithm implementation

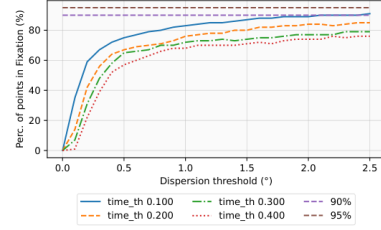


(b) Mean fixation time with the original I-DT algorithm implementation

Percentage of Points Classified Inside a Fixation Plots

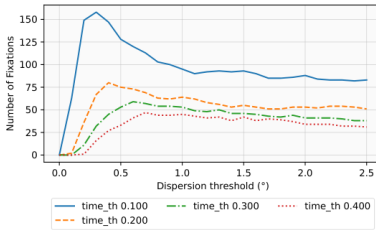


(a) Percentage of points classified as a fixation with the corrected I-DT algorithm implementation

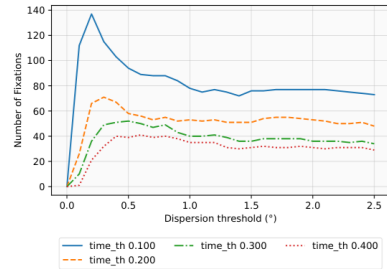


(b) Percentage of points classified as a fixation with the original I-DT algorithm implementation

Number of Fixations Plots



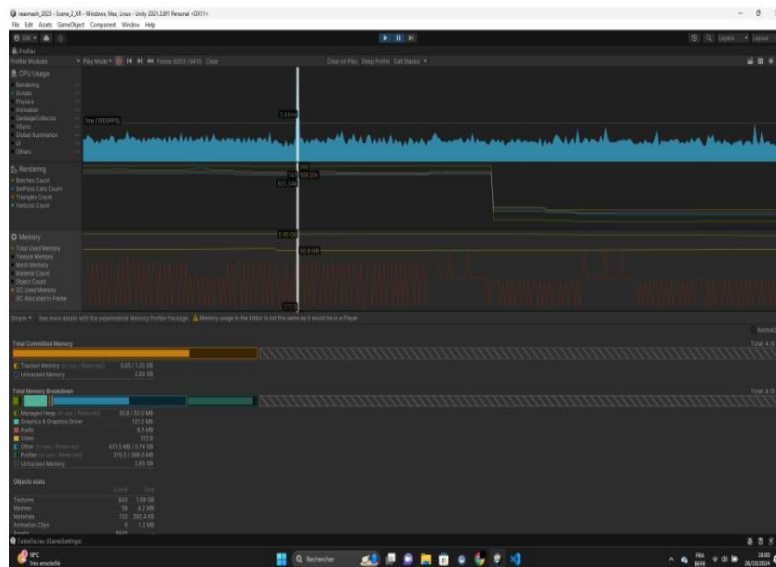
(a) The number of fixations with the corrected I-DT algorithm implementation



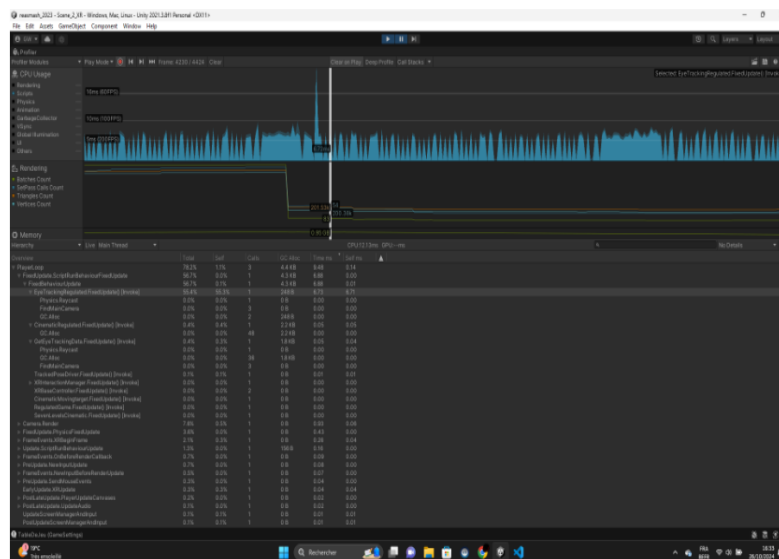
(b) The number of fixations with the original I-DT algorithm implementation

Figure 1. Calibration sweeps. Monotonicity and stability across parameters. The fixation parser exhibits the expected monotonic patterns across dispersion thresholds and stable conclusions within a reasonable neighborhood of parameters.

Chapter 4



Unity's profiler inspection once the script has been disabled



Unity's profiler inspection of the initial integration

Figure 2. Runtime profiling. Before/after SDK callback fix. Profiling identified a callback interaction that degraded performance during gaze collection; after disabling the conflict and revising data handling, acquisition stability was restored.

Chapter 5

Feasibility of a theory-driven dynamic difficulty adjustment algorithm integrating individual performance and normative data for adaptive modulation of spatial and distractor inhibition attention in a non-immersive virtual reality task: Evidence from individuals following Stroke.

Gregorio Sorrentino, Gauthier Everard, Thierry Lejeune And Martin Edwards

Under consideration at

Open Research Europe, submitted April 2026.

DOI: 10.12688/openreseurope.23432.1

Abstract

BACKGROUND: Post-stroke attentional deficits are heterogeneous and may involve both spatial attention impairments, such as unilateral spatial neglect, and non-spatial deficits, including distractor inhibition. Conventional cognitive neurorehabilitation tasks often rely on fixed or manually adjusted difficulty levels to match the level of the patient, which may not adequately accommodate individual variability. Dynamic Difficulty Adjustment (DDA) algorithms offer a performance-driven approach to modulating task demands. The present study examined the feasibility of a theory-driven DDA algorithm integrating individual performance and normative data within a non-immersive virtual reality environment task.

METHODS: A single-group repeated-measures feasibility study was conducted in inpatient and outpatient rehabilitation settings. Ten individuals with stroke completed three 15-minute sessions of DDA-REAsmash. The

Chapter 5

multi-parameter DDA algorithm continuously adjusted stimulus presentation time, distractor inhibition demands, and spatial configuration based on real-time individual performance, aiming to maintain an optimal engagement range of 65-85% success rate. Normative reaction-time percentiles derived from an independent mean age-matched sample were implemented as lower algorithmic constraints. Feasibility was defined as stabilization of performance within predefined engagement boundaries, and adaptive behavior was examined in relation to baseline attentional profiles.

RESULTS: All participants completed the protocol without adverse events. Across sessions, performance converged toward the target engagement range.

CONCLUSIONS: These findings indicate the feasibility of a theory-driven multi-parameter DDA algorithm integrating individual performance and normative data to maintain individualized engagement in a heterogeneous post-stroke sample. Further controlled studies are required to determine clinical efficacy and functional outcomes.

Key words

Stroke, Unilateral Spatial Neglect, Distractor Inhibition, Dynamic Difficulty Adjustment, Serious Games, Virtual Reality, Neurorehabilitation.

Introduction

Despite increasing awareness of the importance of cognitive rehabilitation after stroke, visuospatial attention deficits, such as unilateral spatial neglect (USN)²⁶⁷, are frequently underdiagnosed and often not targeted effectively in rehabilitation programs⁴³. Furthermore, key cognitive functions, such as distractor inhibition, lack in validated assessment and rehabilitation tools⁴³. This under-diagnosis and under-treatment is often linked to limited resources, time constraints, and the shortage of trained neuropsychologists within rehabilitation settings¹⁵⁴. Stroke rehabilitation requires regular and intensive sessions conducted by trained professionals to support functional recovery²⁶⁸.

Psychological factors such as reduced motivation, depression and anxiety, along with fatigue, can further complicate the rehabilitation process²⁶⁹. It is therefore essential to not only guarantee access to high-quality rehabilitation, ensuring adequate treatment intensity, but also to offer engaging and individualized sessions sustaining motivation and preventing dropout^{270,271}.

Digital technologies such as Virtual Reality (VR) Serious Games (SG) have gained growing interest in neurorehabilitation^{268,272}. VR provides structured, interactive, and repeatable environments⁵⁶, with non-immersive VR configurations enabling task execution through screens or touch-based interaction without requiring full sensory immersion^{273,274}. SG consists of entertaining educational training¹⁴³ that can facilitate patient-centered assessment and rehabilitation by encouraging participants to complete challenging and enjoyable tasks²⁷⁵. Research shows that VR SG enhances motivation and increases therapy intensity, further improving sensitivity and standardization in outcome measurement and rehabilitation^{92,268,272}. Like other computerized technologies, VR SG enables the collection of diverse objective and quantitative data, such as behavioral and performance-based outcomes, increasing quantitative measurement sensitivity and specificity^{61,268,272}.

Despite positive evidence in stroke survivors²⁷⁶, the clinical adoption of VR SG for cognitive rehabilitation remains limited¹⁴⁵. One major barrier is the heterogeneity of post-stroke cognitive profiles, with multiple cognitive functions typically affected^{13,110}. This variability makes personalization of rehabilitation particularly challenging, as patients require task demands to be continuously tailored to their individual cognitive abilities²⁷⁷. Conventional VR SG often rely on manual, operator-dependent adjustment of task parameters, usually carried out at the beginning of the session, and with subsequent changes in task difficulty following fixed rules that do not allow for further customization²⁷⁸. Fixed-difficulty tasks often fail to maintain patient engagement, particularly because difficulty is not tailored to the individual's varying abilities. Overly simple tasks reduce motivation

Chapter 5

through being too easy, while overly difficult tasks cause frustration and dropout^{279,280}.

Conventional VR SG for cognitive rehabilitation entails two major practical limitations: (i) it requires trained personnel with sufficient expertise to accurately assess an individual's cognitive deficits and select appropriate task difficulty parameters and (ii), it demands specific training in the use of VR SG software (difficulty adjustment), increasing personnel burden.

To address this limitation, DDA SG have emerged as a promising approach⁹⁰. DDA SG use algorithms to adjust task difficulty based on user performance^{88,91}, aiming to provide challenging yet achievable levels that maintain optimal engagement, typically associated with success rates around 75% (not too easy and not too difficult)^{91,281–283}. Implementing DDA in cognitive rehabilitation requires finely tuned algorithms that are theory-driven and sensitive to latent constructs⁹³.

Within this framework, we developed REAsmash, a modular VR SG grounded in Feature Integration Theory (FIT)⁴⁰. The assessment module of the REAsmash has demonstrated replicable FIT effects, providing an assessment of spatial and non-spatial (distractor inhibition) visual-attention, and motor control in post-stroke and healthy populations in both immersive and non-immersive VR versions^{95,132,219,220}. Here, we present a new REAsmash module implementing a DDA algorithm designed to provide individualized, theory-driven cognitive rehabilitation. A fully immersive VR version of DDA-REAsmash was recently used by Everard et al.²⁶¹ to study motor learning in healthy older adults (with the DDA algorithm specifically designed to support motor learning). In this study, task difficulty was continuously adjusted to individual performance across training sessions, resulting in improvements in response speed, accuracy, movement smoothness, and manual dexterity, with retention and transfer to untrained tasks. In contrast, the present study introduces a novel, theory-driven DDA algorithm tailored to post-stroke cognitive rehabilitation, targeting spatial and non-spatial attentional deficits in a non-immersive VR setting. This new module introduces an additional innovation in DDA-SG design by

integrating normative performance data from age-matched healthy controls within the DDA update rules, extending standard DDA approaches that rely solely on individual performance²⁸⁴.

Based on previous findings and FIT, three hypotheses were formulated.

(i) Feasibility: The DDA-REAsmash will maintain performance within an optimal engagement range of 65-85% success rate (i.e., centered around the mean of 75%).

(ii) Adaptability: To maintain the optimal success rate, the DDA algorithm will modulate task difficulty as a function of individual participant performance.

(iii) We expect DDA-REAsmash to modulate task parameter difficulty to each participant's cognitive profile, leading to a progressive stabilization of cognitive demand, reflecting clinically interpretable parameters. We expect longer stimulus presentation durations in individuals presenting impaired distractor inhibition, and we expect spatial configuration adjustment in individuals presenting lateralized visuospatial deficits.

Materials and methods

Study design

This study employed a prospective single-group repeated-measures feasibility design. The objective was to examine the short-term behavior of a theory-driven DDA algorithm integrating individual and normative data within a non-immersive virtual reality environment. The study was conducted in accordance with the STROBE guidelines¹⁵⁰ for observational studies, and the intervention description followed the TIDieR framework²⁸⁵.

The study is part of a broader research program registered on ClinicalTrials.gov (NCT04694833); the registry reflects the overall study timeline, while recruitment for the present feasibility phase evaluating the DDA-REAsmash module took place between November 2024 and June 2025.

Chapter 5

Participants

Given the feasibility design of this study, no formal *a priori* sample size computation was performed. Sample size was instead informed by previous work on the FIT interaction underlying the DDA algorithm. *A priori* study using the non-immersive REAsmash assessment module⁹⁵ reported a large within-participant FIT effect ($\eta^2 = 0.487$; Cohen's $f \approx 0.97$). Based on this effect size, a power estimate suggested that nine participants would be sufficient to detect the effect with 80% power at $\alpha = 0.05$. To account for potential dropouts, ten participants were recruited.

Participants were recruited from the physical medicine and rehabilitation department of the *Cliniques universitaires Saint-Luc* in Brussels and were either currently hospitalized or already discharged. Recruitment took place from November 2024 to June 2025. The post-stroke participants were selected using the following inclusion criteria: (1) adult participants (i.e., minimum age of 18 years old); (2) presence of an ischemic or hemorrhagic first cortical and / or sub-cortical stroke, diagnosed by CT or magnetic resonance imaging; and (3) a good understanding of the task instructions. The exclusion criteria were: (1) uncorrected vision deficiencies; (2) presence of other neurological conditions (e.g., major neurocognitive disorder or extrapyramidal disorders) that could bias the outcomes; (3) medication-resistant epilepsy; (4) orthopedic dysfunction that could influence upper extremity function; and (5) too poor trunk control to sustain the trial.

All participants were screened for visual USN. The assessment included a standardized battery of gold-standard tests: the Bells Test³⁰, the Broken Hearts Test³¹, and Visual Field and Visual Scanning subtests from the computerized Test for Attentional Performance (TAP) battery¹³¹. The complete gold-standard assessment session also included the Go/NoGo subtest of the TAP and the Montreal Cognitive Assessment (MoCA)⁴⁶ and lasted approximately 40-60 minutes. All participants also completed one session of the non-immersive REAsmash assessment module to estimate individual distractor inhibition deficits.

Assessment time windows were chosen *a priori* to balance clinical feasibility with the need to ensure that baseline assessments reflected participants' current functional status. Participants in the subacute phase underwent the assessment within 10 days prior to the DDA-REAsmash sessions to minimize confounding effects of rapid spontaneous recovery and clinical fluctuations that are most prominent in the early post-stroke period²⁸⁶, participants in the chronic phase were assessed within up to 30 days.

Materials

The DDA-REAsmash runs on the REAtouch[®] (Axinesis[®]), a non-immersive VR medical device. The REAtouch[®] consists of a 43" interactive touch-sensitive screen (95 × 53 cm) mounted on a motorized structure that allows for customizable height adjustment and screen inclination (Figure 1).

Chapter 5



Figure 1. The non-immersive VR device. *The REAtouch® system consists of a 43-inch interactive touchscreen mounted on an adjustable support structure allowing customization of height and inclination. In the present study, the screen was positioned horizontally (0° inclination). Participants interacted directly with the touchscreen to perform the visual search task. Photograph taken by the authors.*

The DDA-REAsmash module maintains the graphical design of the REAsmash assessment module. It features a cartoon-style visual display and an active playing area measuring 95×45 cm. The playing field can present up to 24 molehills arranged in a 6×4 grid, with moles simultaneously emerging from different molehills. Each mole and molehill covers an area of 8×8 cm. The target mole is identified by a red miner's helmet, while distractor moles have blue miner, blue horned, or red horned helmets.

The DDA task parameters included (i) the number and distribution of the molehills (i.e., the active playing field), (ii) distractor salience and number, (iii) stimuli presentation time, and (iv) cues designed to attract attention to

the target (i.e., spatial auditory cues, and visual cues, each progressively simplifying the task difficulty relative to the no-cue condition). The first 12 trials served as a baseline block presenting an ‘easy’ starting point. The presented stimuli had minimal task demands, with a reduced active playing field consisting of eight molehills arranged in a 4×2 grid centered close to the participant. In this initial phase, only the target mole was presented (requiring no distractor inhibition), and the target remained visible for 10 seconds (maximum duration), with cues set at maximum intensity (helping the participant to find the target).

All DDA parameters were then updated after each block of 12 consecutive trials, enabling the system to adjust task difficulty at regular intervals based on mean individual performance across the previous 12 trials. Each parameter was designed to stabilize a specific performance dimension corresponding to the individual’s profile, and together these adaptive mechanisms aimed to maintain an overall success rate of approximately 75% (i.e., with difficulty specific to the individual’s profile and allowing the individual to find the target on 75% of trials). For the active playing field, the DDA algorithm dynamically adjusted the spatial configuration of the molehills based on the participant’s spatial performance profile. Specifically, the algorithm used the spatial distribution of omissions to reshape the active playing field, progressively modifying its size and lateral balance in order to maintain an optimal challenge level while targeting individual visuospatial limitations. Targets were presented in a semi-randomized manner, appearing at least twice in each active column per block and never twice in the same molehill (except when a column contained a single molehill). This procedure ensured spatial unpredictability while allowing the detection of systematic lateralized response biases, such as increased omissions when targets appeared in the contra-lesional hemifield relative to the brain lesion. When such lateralized omissions are detected, the DDA is expected to adjust the shape of the playing field by reducing target density in the most impaired spatial regions while maintaining a limited number of molehills within the neglected hemifield. This spatial manipulation was designed to challenge participants with a

Chapter 5

playing area slightly exceeding their current visuospatial and/or motor range, rather than fully excluding the impaired space.

For example, in individuals with unilateral spatial neglect, the DDA progressively shifted the active playing field toward the ipsi-lesional side while preserving a small proportion of targets in the contra-lesional hemifield. This configuration allowed the system to maintain the target success rate around 75% while simultaneously promoting engagement with the neglected space, thereby directly targeting the participant's spatial attentional bias.

The number and type of distractors were chosen based on the FIT effect. The FIT effect relies on a contrast between high versus low target-distractor salience and the number of distractors. The red-helmet distractors create low target-distractor salience with the red-helmet target (differing by the shape of the helmet) and evoke serial visual search when searching for the target's spatial location amongst distractors. In low target-distractor salience conditions, increased numbers of distractors progressively increase cognitive load and increase the need for distractor inhibition^{132,219,220}. In contrast, the high target-distractor salience conditions (red-helmet target amongst blue-helmet distractors) require little distractor inhibition and are not influenced by increasing distractor number (Figure 2).



Figure 2. The different stimuli of the DDA-REAsmash. *The target mole is identified by a red miner's helmet. Distractor moles wore blue miner's helmets, blue horned helmets, or red horned helmets. The presentation of the target with only distractor moles wearing blue helmets created high salience conditions with low inhibition demands. The presentation of the target with distractor moles wearing red and blue helmets created low targetdistractor salience conditions, requiring greater inhibition demands relative to the high salience conditions.*

By manipulating target-distractor salience (features) and distractor number, the DDA algorithm can modulate distractor inhibition demands (difficulty). After an initial presentation with an incremental number of high-salience distractors, low-salience distractors were progressively introduced to increase the cognitive load through distractor inhibition. If a participant already showed reduced accuracy with high target-distractor salience conditions (i.e., only blue distractors), red distractors were not introduced by the DDA to prevent overload due to low target-distractor salience (i.e., too much difficulty). Conversely, when the overall success rate dropped below the target range, the algorithm analyzed the type of distractor most frequently associated with errors and progressively reduced their occurrence, maintaining an adaptive balance between challenge and performance stability.

Chapter 5

To ensure the task remained appropriately challenging, especially under high distractor inhibition demands, stimuli presentation times were calibrated by the DDA using normative response time data from healthy controls tested with the non-immersive VR assessment module⁹⁵. Specifically, lower bounds were derived from the 75th percentile of response times observed in low-salience levels of the assessment version. The 75th percentile of response times represents the minimum duration required for individuals without distractor inhibition deficits to correctly find the target in 75% of trials. These bounds were then estimated for different conditions varying in the number of red distractors. The full DDA algorithm description is provided as Extended Data 1 (“Full DDA algorithm description”), including step-by-step mathematical specifications of the computation of minimum stimulus presentation times, the derivation of normative performance constraints, and the explicit rule-based update equations governing all DDA parameters, enabling independent replication of the adaptive procedure.

At the end of each block, a 10-second pause was provided. During this pause, the touch-sensitive screen displayed feedback scores related to the completed block, including success rate, number of errors, and number of omissions. At the end of each session, an animation provided rewarding feedback with festive music and the achievement of a new personal best or a virtual medal linked to the number of levels played.

Procedure

The study was conducted in a clinical testing room at the *Cliniques universitaires Saint-Luc*, Brussels. All sessions were conducted by the first author of the study (PMR specialist), who was the intervention provider for the project. Participants were seated either on a standard four-legged office chair or in their own wheelchair. They were positioned in front of the REAtouch[®] and aligned with the sagittal axis of the interactive screen. The inclination and height of the interactive screen was set at 0° and 74 cm.

Prior to the first 12 trials block, participants were instructed to “smash” the target mole as quickly and accurately as possible using their less impaired hand. Before the task, the examiner provided oral instructions supported by a standardized visual presentation illustrating task instructions and stimulus examples. Immediately before the session, a short-written sentence and an audio prompt appeared on the touch-sensitive screen, inviting the participant to find and respond to the mole as quickly as possible. At the start of each trial, participants had to place their response hand on an “X” superimposed at the center-lower edge of the screen, ensuring a consistent starting position. The “X” disappeared immediately after touching it and the trial began.

Omissions referred to missed targets (i.e., the participant was unable to hit the target within the presentation time). Errors were recorded when participants responded to and touched a distractor. Different types of auditory feedback were associated with positive or negative responses. Each session lasted 15 minutes. Participants completed three training sessions over one week.

Outcomes

The primary outcome testing the feasibility hypothesis was the success rate per 12-trial block, defined as the percentage of targets correctly found within each block. This measure was used to assess whether DDA-REAsmash could adjust task difficulty in order to maintain individual participant performance success within the optimal engagement range of 65-85%^{91,281-283} (mean 75%).

Adaptability was evaluated using a Composite Difficulty Index. The Composite Difficulty Index provides a quantitative measure of task difficulty by integrating the three dimensions most relevant to cognitive load modulation in DDA-REAsmash. Specifically, it combined stimuli presentation time, the number of low-salience distractors, and the size of the active playing field. Shorter presentation times, a higher number of red distractors, and larger playing fields contributed to increased composite

Chapter 5

difficulty. Each component was normalized relative to its predefined theoretical or observed range, yielding Composite Difficulty Index values between 0 and 1, with higher values indicating greater difficulty. The index reflects how the DDA algorithm balances visual search load, inhibition demands, and spatial complexity across successive blocks, representing each participant's individualized task difficulty trajectory. A detailed explanation and operational description of the Composite Difficulty Index is provided as Extended Data 2 ("Composite Difficulty Index formalization").

A further assessment of adaptability was assessed by analyzing stimuli presentation time and active playing field configuration across blocks to examine whether adaptive adjustments aligned with individual participant clinical profiles for distractor inhibition and visuospatial attention impairments (i.e., to examine whether adaptive parameter adjustments corresponded to attentional profiles).

Data analysis

Statistical analyses were conducted in R (version 4.4.0). All derived metrics and modeling procedures were implemented using reproducible R scripts. No proprietary statistical software was required.

Success rates were calculated per 12-trial block and per participant. The feasibility of the DDA-REAsmash algorithm was assessed using two analyses. Firstly, Chi-square goodness-of-fit tests were performed on the total counts of successes versus non-successes (errors and omissions) for each participant across blocks. Secondly, one-sample t-tests ($\alpha = 0.05$, two-tailed) were applied to block-wise success rates to verify deviations from the expected 75% target, thereby allowing the identification of stabilization around the target range of 75% (early blocks with significant deviations and later blocks showing stabilization).

Adaptability was evaluated using the Composite Difficulty Index score. For each participant, block-wise Composite Difficulty Index scores were computed to track the evolution of task difficulty over time on a continuous scale from 0 (minimum difficulty) to 1 (maximum difficulty). To

characterize how difficulty changed across successive blocks, Composite Difficulty Index trajectories were modeled using an asymptotic growth function:

$$\gamma(x) = a + b(1 - e^{-c \cdot x})$$

where a represents the initial difficulty level, b the gain from baseline to plateau, and c the adaptation rate. Model parameters were estimated using nonlinear least squares fitting implemented in R. This modeling approach enables the identification of potential plateaus in the difficulty curves, providing model-based estimates of each participant's task difficulty stabilization level. Plateau stabilization was interpreted as consistent with algorithmic convergence toward individualized engagement bounds.

Analysis of individualized adaptability used two separate analyses. These analyses explored patterns in the adaptive responses of DDA-REAsmash in relation to two distinct cognitive deficits: (i) distractor inhibition impairment and (ii) USN-related lateral bias. The first analysis assessed whether participants with distractor inhibition difficulties required longer stimulus presentation durations. To detect impairments in distractor inhibition, participants were classified according to the number of omissions across the three low-salience levels of the REAsmash assessment module. Because omissions may also result from attentional lateral bias, for participants identified with USN using gold-standard tests, omissions were attributed to pure attentional lateral bias when they occurred exclusively in the contra-lesional field. Accordingly, these participants were considered not to exhibit distractor inhibition deficits (i.e., zero omissions attributed to distractor inhibition impairment). Participants with USN were considered to have concurrent distractor inhibition difficulties if omissions occurred in the ipsi-lesional field were more than one and accounted for over 25% of total omissions. Participants with USN and less than 25% of omissions, or only one omission, in the ipsi-lesional field were not included in this analysis.

To characterize adaptation over time, stimuli presentation durations for each participant were analyzed using asymptotic growth functions. A Spearman

Chapter 5

rank correlation analysis was then conducted between distractor inhibition impairment (i.e., omission count in the assessment module) and the stabilized stimulus presentation time in the DDA-REAsmash.

The second analysis explored whether participants with USN-related lateral bias specifically exhibited asymmetric adjustments of the active playing field, quantified as the percentage of molehills displayed in the contra-lesional hemifield relative to the total. For this analysis, participants were classified based on gold-standard USN assessments and omission lateralization at the assessment module into three groups: individuals with USN at the gold standard tests and no omissions in the ipsi-lesional hemifield, individuals with USN and concurrent omissions in the ipsi-lesional hemifield, and participants without USN. Temporal changes in the percentages of molehills displayed in the contra-lesional hemifield were analyzed using asymptotic growth functions.

Results

None of the participants asked to interrupt the session or withdraw from the project. The sessions were well tolerated and overall described as non-stressful and engaging. No participants asked to stop the experiment prematurely or to extend the rest periods.

The participants consisted of 7 males and 3 females, with a mean age of 56 years ($SD=12.0$). All participants were VR naïve and 6 reported that the less impaired hand (i.e., the response hand) was their pre-stroke dominant hand. The average time since stroke was 14 months ($SD=15.0$ months), with 4 participants in sub-acute phase (i.e., within 6 months from the stroke) and 6 in chronic phase, and 8 with ischemic stroke, 1 with hemorrhagic stroke, and 1 with ischemic stroke complicated by hemorrhagic transformation. Lesions primarily affected the Sylvian regions in all participants and were - located in the right hemisphere in 6 participants. The mean MoCA score was 25.7 ($SD= 1.6$). Rehabilitation status varied, with all participants still undergoing neuropsychological, occupational, and/or physical therapy at the time of testing. In the REAsmash assessment module, omission rates ranged

from 0 to 5 in the low target-distractor saliency levels, with higher omission rates indicating more severe deficits in distractor inhibition. Three participants exhibited signs of USN on the gold-standard tests. See Table 1 for demographic and clinical characteristics of the participants. Detailed results of the gold-standard assessments for spatial attention are provided as Extended Data 3.

All participants completed the training sessions without adverse events.

Table 1. Demographic and clinical characteristics of participants (de-identified).

ID	Sex	Age (years)	The response was made with the pre-stroke dominant hand?	Stroke phase	Stroke type	Brain lesion side	Omission count in the assessment module	Current spatial attention impairment	Rehabilitation status
P1	M	60–69	No	Chronic	Hemorrhagic	Left	2	No	Ongoing rehabilitation
P2	M	50–59	Yes	Chronic	Ischemic	Right	3	Yes	No rehabilitation
P3	M	50–59	Yes	Chronic	Ischemic	Right	5	Yes	Ongoing rehabilitation
P4	F	50–59	No	Chronic	Ischemic	Left	0	No	Ongoing rehabilitation
P5	M	50–59	Yes	Chronic	Ischemic	Right	0	No	Ongoing rehabilitation
P6	F	70–79	Yes	Chronic	Ischemic	Right	1	No	Ongoing rehabilitation
P7	M	60–69	Yes	Subacute	Ischemic	Right	1	No	Ongoing rehabilitation
P8	M	50–59	No	Subacute	Mixed	Left	1	No	Ongoing rehabilitation
P9	M	60–69	No	Subacute	Ischemic	Left	5	No	Ongoing rehabilitation
P10	F	20–39	Yes	Subacute	Ischemic	Right	3	Yes	Ongoing rehabilitation

F = Female, M = Male.

Chapter 5

Feasibility

Participants completed an average of 48.5 (SD = 7.12) blocks across the three sessions. Participants required 5.4 (SD = 1.07) blocks on average to reach the 65-85% target range (hereon labelled as pre-target range blocks). Chi-square goodness-of-fit tests on overall success versus non-success counts across all blocks showed a significant deviation from the expected 75% success rate for one participant ($\chi^2 = 16.79$, $p < .001$), while the other nine participants aligned with the expected distribution. When analyses were restricted to blocks following the first in-range block (i.e., pre-target range blocks exclusion), this same participant continued to show a significant deviation ($\chi^2 = 6.92$, $p = .009$), whereas no significant deviations were observed for the remaining participants ($p \geq .22$).

One-sample t tests comparing observed success rates to the 75% target across blocks showed that pre-target range blocks exceeded the target range, with mean success rates of 100% for blocks 1 and 2 and 94-99% for blocks 3 and 4 ($p < .001$). One-sample t tests on blocks following the pre-target range blocks indicated a significant deviation for a single participant, ($t(53) = 2.35$, $p = .023$), with all others non-significant ($p > .05$) (see Table 2 and Figure 3).

Table 2. Mean success rates and inferential statistics relative to the 75% target performance.

ID	Mean success rate	SD	t-test	t-test p-value	Chi-square	Chi-square p-value
P1	74.8%	0.196	-0.061	0.951	0.009	0.923
P2	75.0%	0.180	0.000	1.000	0.000	1.000
P3	79.5%	0.140	2.350	0.023	6.922	0.009
P4	73.6%	0.240	-0.375	0.709	0.519	0.471
P5	73.4%	0.154	-0.676	0.503	0.694	0.405
P6	72.7%	0.218	-0.691	0.493	1.455	0.228
P7	73.0%	0.222	-0.556	0.582	0.973	0.324
P8	76.1%	0.127	0.643	0.523	0.427	0.513
P9	74.2%	0.139	-0.317	0.753	0.125	0.724
P10	73.1%	0.153	-0.725	0.473	0.790	0.374

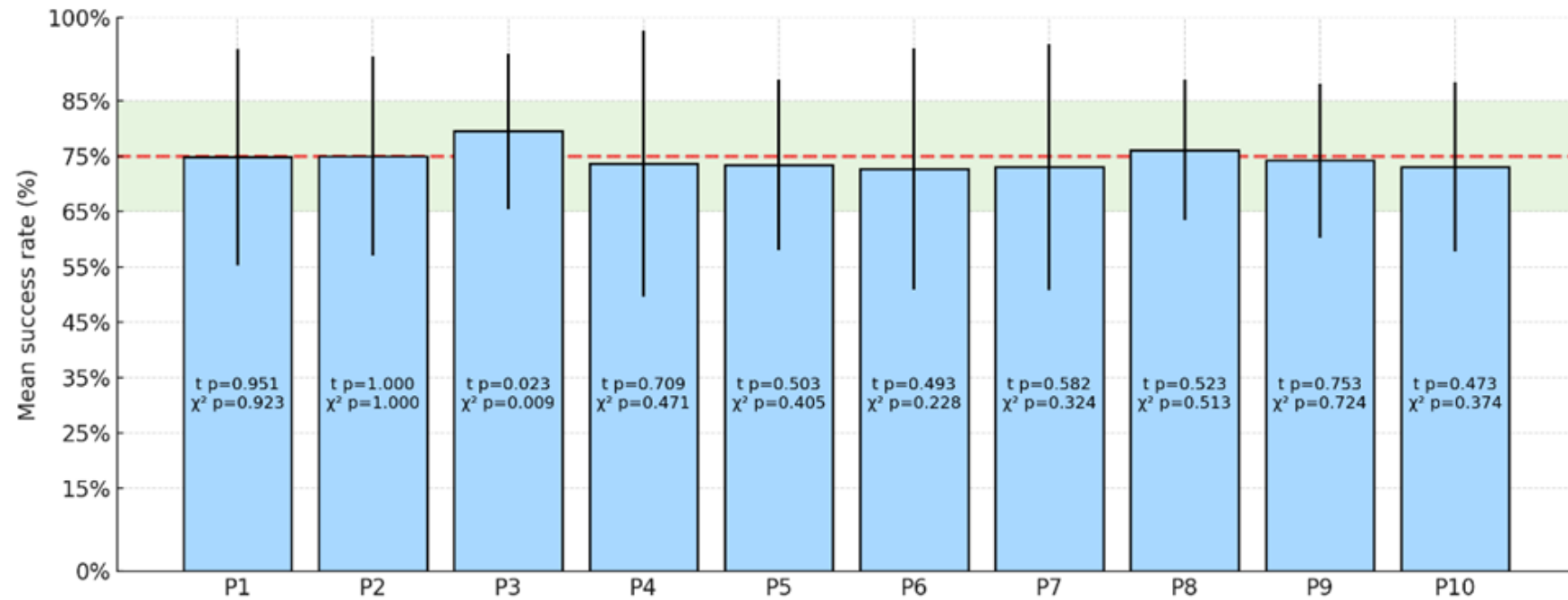


Figure 3. Individual block-wise success rates, excluding warm-up blocks, across participants. Each bar represents the mean success rate across blocks after exclusion of initial blocks required to reach the target engagement range. The dashed horizontal line indicates the 75% target success rate, and the shaded area represents the predefined engagement range (65-85%). Error bars denote standard deviation

Chapter 5

Adaptability

Composite Difficulty Index trajectories showed, in all participants, a rapid early change in difficulty adjustment followed by stabilization over successive blocks. Plateau values ranged between 0.7 and 0.9, indicating individual task difficulty levels (i.e., the difficulty level required for the individual to successfully find the target on 75% of trials). These difficulty levels depend on the performance profiles of each individual. The fitted curves suggest similar adaptation patterns across participants, with consistent stabilization patterns observed across trajectories (Figure 4).

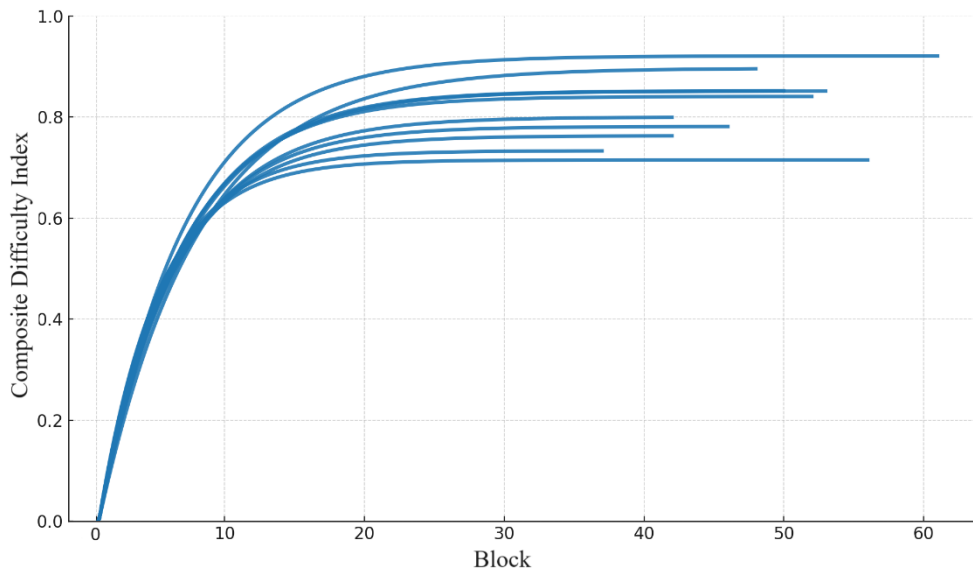


Figure 4. Composite Difficulty Index trajectories across participants. The X-axis represents the block number (i.e., progression over successive blocks), and the Y-axis represents the Composite Difficulty Index, ranging from 0 (minimum difficulty) to 1 (maximum difficulty). Each curve shows the evolution of task difficulty over time in one participant. The duration of the study was fixed (i.e., 15 minutes per session), causing the number of blocks completed by the individual to vary depending on their speed of performance.

Individualized Adaptability

DDA-REAsmash for distractor inhibition rehabilitation

For the estimation of distractor inhibition impairment, participants were classified according to the number of omissions across the three low-salience levels of the REAsmash assessment module: no omissions (2 participants), one (3 participants), two (1 participant) three (2 participants), and five omissions (2 participants).

In participants with USN, omissions were examined with respect to their spatial distribution, since contra-lesional omissions are typically attributed to lateralized attentional bias. One of the three participants with USN showed three omissions, all confined to the contra-lesional hemifield, consistent with pure attentional lateral bias. This participant was therefore considered as not showing distractor inhibition deficits (i.e., zero omissions attributed to distractor inhibition). In the remaining two participants with USN, omissions occurred in both hemifields. However, in only one, the omissions in the contra-lesional hemifield accounted for less than 75% of the total omissions (i.e., 1 out of 3 total omissions), meeting the criterion for concurrent spatial and distractor inhibition difficulties. The third participant showed four omissions in the contra-lesional hemifield and only one in the ipsi-lesional hemifield and was therefore excluded from this distractor inhibition analysis.

A strong positive correlation was observed between the number of omissions in the assessment module and the stabilized stimulus presentation time in the DDA-REAsmash (Spearman's $\rho = 0.97$, $p < 0.001$). Participants with higher omission rates required longer presentation durations (to obtain 75% correct performance) (Figure 5).

Chapter 5

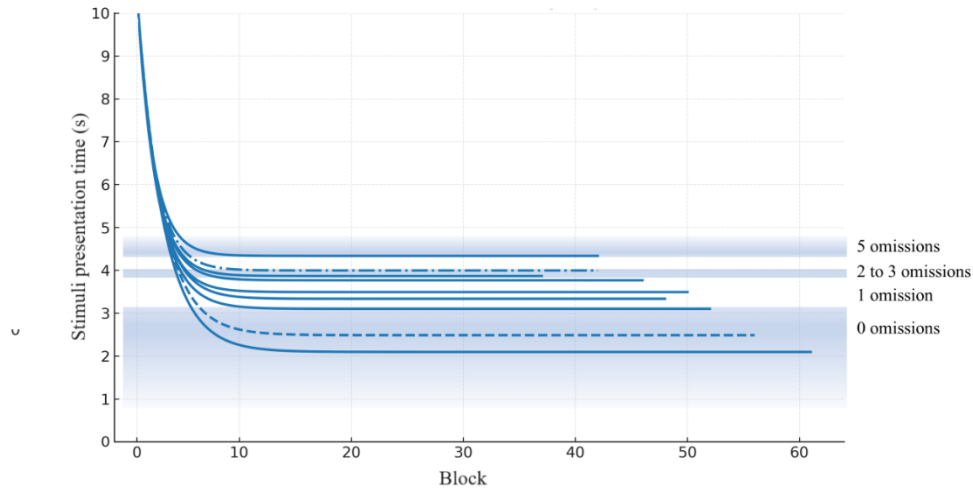


Figure 5. Relationship between stabilized stimuli presentation time and omission number. The figure illustrates the evolution of stimuli presentation time across successive blocks for each of the 9 participants included in this analysis. The X-axis presents the block number, and the Y-axis presents the stimulus presentation time (in seconds) determined by the DDA. The shaded horizontal bands highlight clusters of stabilized presentation times corresponding to different omissions obtained in the REAsmash assessment module (values shown on the right). The dash-dotted line presents the participant who exhibited both USN and distractor inhibition impairment, while the dashed line corresponds to the participant with USN only, whose omissions were not related to distractor inhibition.

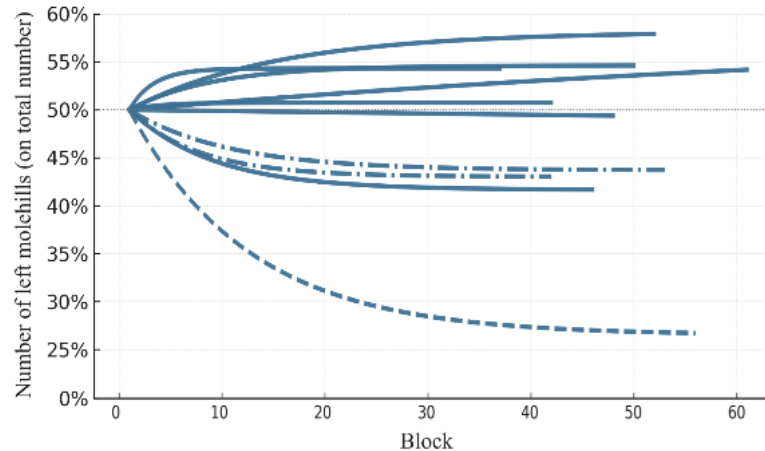
DDA-REAsmash for attentional lateral bias rehabilitation

For the analysis examining the algorithm's ability to detect and target attentional lateral bias, participants were categorized into three groups: (i) pure USN-related lateral bias based on gold-standard tests, with no concurrent omissions in the ipsi-lesional hemifield (1 participant); (ii) USN with omissions in both the contra- and ipsi-lesional hemifields (2 participants); and (iii) no USN (7 participants).

The DDA algorithm for the participant with pure USN lateral bias adapted to the active playing field, and showed less targets in the contra-lesional space, showing a lateralized adaptation pattern. The percentage of molehills in the contra-lesional (left) hemifield stabilized slightly above 25% of the total. In contrast, the remaining participants showed values close to symmetry between the two hemifields (Figure 6).

Chapter 5

a.



b.

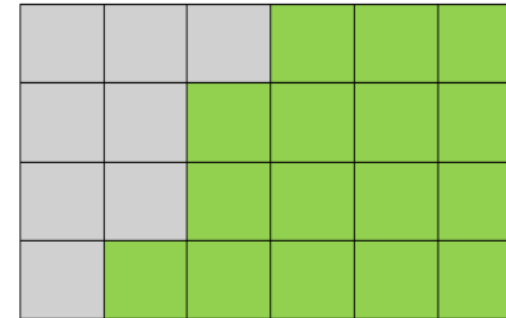


Figure 6. Adaptation of the active playing field in relation to attentional lateral bias. (a) Percentage of molehills presented in the left hemifield relative to the total, plotted across blocks. The X-axis presents block number, and the Y-axis presents the proportion of molehills displayed on the left side of the playing field relative to the total number of molehills. The dashed line corresponds to the participant with USN and no concurrent omissions in the ipsi-lesional hemifield. The two dash-dotted lines represent participants with USN and concurrent spatial and distractor inhibition difficulties. Continuous solid lines correspond to participants without USN. **(b)** Schematic representation of the active playing field of the participant with USN and no concurrent distractor-inhibition deficits. Green rectangles indicate the molehills selected by DDA-REAsmash as the configuration to challenge the participant's attentional lateral bias, whereas grey rectangles represent inactive areas of the playing field in which no molehills were presented.

Discussion

The present study evaluated the feasibility and adaptive behavior of DDA-REAsmash, a non-immersive VR SG implementing a theory-driven multi-parameter DDA algorithm integrating individual and normative performance data within a heterogeneous group of post-stroke individuals. All participants completed the protocol without adverse events, indicating good tolerability.

Concerning feasibility, individual- and group-level performance data showed rapid stabilization of success rates within the predefined optimal engagement range (65-85%). Success rates converged toward the 75% target after an average of 5.4 blocks, corresponding to approximately 2.5 minutes of gameplay. Although one participant showed a statistically significant deviation in inferential analyses, the observed mean success rate remained within the predefined engagement range. Overall, these findings are consistent with algorithmic convergence toward predefined engagement bounds.

Analyses of adaptability using the Composite Difficulty Index showed a rapid early increase in task difficulty followed by individualized plateau stabilization across participants. All participants began at minimal task demand, and the DDA progressively modulated stimulus presentation time, distractor inhibition load, and spatial configuration of the active playing field. The plateau levels were consistent with the level of difficulty required to maintain approximately 75% correct performance.

A central characteristic of the present implementation was the integration of normative performance from an independent sample of healthy participants within the DDA difficulty moderation rules. Lower limits for stimulus presentation time were derived from the 75th percentile of response times observed in the mean age-matched healthy controls and implemented as algorithmic constraints. This integration anchored parameter modulation to empirically derived performance distributions and was designed to constrain parameter drift driven solely by intra-individual variability.

Chapter 5

The relationship observed between omission counts in the assessment module and stabilized stimulus presentation times further illustrated individualized adaptive modulation. Participants with higher omission rates in low-salience conditions stabilized at longer presentation times, whereas participants with fewer omissions stabilized at shorter durations. These findings suggest that stimulus presentation time was modulated in relation to individual distractor inhibition characteristics during serial visual search.

With regard to spatial attention, most participants showed that the DDA maintained symmetrical configurations of the active playing field across blocks. In contrast, the participant presenting pure USN showed that the DDA made a progressive ipsi-lesional lateralization of the active playing field. Early blocks began with symmetrical presentation, but contra-lesional lateralized omissions (typical for USN) influenced subsequent spatial parameter adjustments, leading to a stimuli configuration having most stimuli presented in ipsi-lesional hemifield, and only a few stimuli presented in the contra-lesional hemifield, thereby to maintaining performance within engagement bounds (i.e., only the right molehills proximal to the playing field midline were displayed). In this case, spatial modulation allowed difficulty stabilization under lateralized attentional constraints.

In participants presenting concurrent spatial and distractor-inhibition impairments, adaptive adjustments involved multiple task parameters without a predominant spatial shift. Stimulus presentation time modulation appeared sufficient to stabilize performance, reducing the need for marked spatial reconfiguration. This pattern is consistent with parallel modulation across multiple attentional dimensions rather than isolated adjustment of a single domain.

Taken together, these results describe a multi-parameter adaptive mechanism capable of modulating visual search load, inhibitory demand, and spatial configuration in parallel. Unlike fixed-difficulty implementations or manually preset session-level adjustments, the DDA-REAsmash continuously updated task parameters according to explicit algorithmic rules integrating both real-time performance and normative

constraints. The primary contribution of this study lies in the characterization of these algorithmic trajectories within a feasibility framework.

From a translational perspective, stabilized adaptive parameters such as stimulus presentation time and spatial field distribution provide quantitative descriptors of attentional processing during controlled task performance. Further investigation is required to determine whether changes in these parameters reflect learning, recovery processes, or task-specific adaptation. The adaptive framework described here may provide a methodological basis for future adaptive serious games targeting heterogeneous cognitive deficits in neurorehabilitation.

Limitations and Directions for Future Research

The study was not designed to evaluate clinical efficacy, transfer effects, or long-term learning. No comparison with fixed-difficulty training was performed. The small sample size limits precision of effect estimates and generalizability. Future randomized controlled trials with larger cohorts will test the efficacy of DDA-REAsmash against fixed-difficulty training. Planned protocols will extend to three sessions per week over four weeks, with follow-up to assess retention, transfer, and functional impact. Further studies will explore multimodal rehabilitation (e.g., cognitive-motor coupling) and performance using the more impaired hand as response hand.

The non-immersive setting was chosen based on prior REAsmash (assessment module) findings⁹⁵ showing that immersive VR increases extraneous load in patients with attentional deficits. Direct comparisons between immersive and non-immersive DDA-REAsmash versions are needed to clarify how sensory load and user experience influence rehabilitation outcomes.

Conclusions

This study demonstrates the feasibility of a theory-driven multi-parameter DDA algorithm integrating individual performance normative data in a

Chapter 5

heterogeneous post-stroke sample. The algorithm maintained performance within predefined engagement bounds and generated individualized adaptive trajectories coherent with baseline attentional profiles. These findings describe algorithmic behavior within a feasibility framework. Controlled studies are required to assess clinical efficacy and functional outcomes.

Declarations

Ethics approval and ethical compliance

The study received approval from the Saint Luc UCLouvain Clinical Ethics Committee (reference: 2015/10FEV/053) and was conducted in accordance with the principles of the Declaration of Helsinki and its later amendments. The protocol was prospectively registered on ClinicalTrials.gov (Identifier: NCT04694833).

Informed consent

All participants volunteered to participate in the study providing written informed consent prior to enrollment. Participants received detailed written and oral information regarding study objectives, procedures, potential risks, and their rights, including the right to withdraw at any time without impact on their clinical care.

Consent for publication

Not applicable, as no identifiable individual data are included in the manuscript or associated materials.

Data availability

Underlying data

Underlying data are openly available from the UCLouvain Dataverse repository:

Sorrentino, Gregorio, 2026. Replication Data for: Feasibility of a theory-driven dynamic difficulty adjustment algorithm. Open Data @ UCLouvain. <https://doi.org/10.14428/DVN/EZR1JX>

Data are available under the Creative Commons Attribution-ShareAlike 4.0 International (CC BY-SA 4.0) license. The repository contains fully de-identified participant-level and trial-level data supporting the analyses presented in this study. All data were de-identified in accordance with the Safe Harbor method (U.S. Department of Health & Human Services)²⁸⁷, and indirect identifiers were generalized to minimize re-identification risk. For further information regarding the dataset, readers may contact the corresponding author.

Extended data

Extended methodological details and additional materials are available from the same repository: <https://doi.org/10.14428/DVN/EZR1JX>

All extended data are provided in de-identified form and are available under the Creative Commons Attribution-ShareAlike 4.0 International (CC BY-SA 4.0) license.

This repository contains the following materials:

- Detailed description of the Dynamic Difficulty Adjustment (DDA) algorithm, including parameter update rules and computational procedures enabling independent replication.
- Formalization of the Composite Difficulty Index, including normalization procedures and mathematical definitions across temporal, spatial, and distractor-related dimensions.

Chapter 5

- De-identified participant-level data from gold-standard neuropsychological assessments (e.g., MoCA, Bells Test, Broken Hearts Test, TAP subtests).
- Informed consent form (English version, de-identified template approved by the local ethics committee), provided for transparency purposes.

Software Availability

The DDA-REAsmash framework is implemented within a research software platform developed at UCLouvain, tightly integrated with proprietary hardware (REAtouch®, Axinesis), and is therefore not distributed as standalone code. For this reason, the source code is not publicly available. However, to ensure transparency and reproducibility, a complete description of the algorithm, including parameter definitions, update rules, and computational procedures, is provided in the manuscript and Extended Data. This level of detail enables independent replication of the adaptive algorithm without access to the proprietary implementation. For further information, readers may contact the corresponding author.

Reporting guidelines

The STROBE and TIDieR reporting checklists have been completed and are available in the UCLouvain Dataverse repository. Repository: UCLouvain Dataverse

DOI: <https://doi.org/10.14428/DVN/EZR1JX>

Data are available under the terms of the Creative Commons Attribution-ShareAlike 4.0 International (CC BY-SA 4.0) license.

Author contributions

GS conceived the study, performed the analyses and drafted the manuscript. GE, TL and ME contributed to the development of REAsmash, interpretation of the results and critical revision of the manuscript.

All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Grant Information

This article is based upon work from COST Action CA24123 - Extended Reality Neurorehabilitation of Spatial Neglect and Related Disorders After Brain Injury (neuroXRehab), supported by COST (European Cooperation in Science and Technology).

Acknowledgments

We thank Julien Sapin (AXINESIS) for providing help and support with the REAtouch® device.

Chapter 5

Extended material 1

DDA Algorithm Description

The DDA algorithm dynamically adjusts task demand (difficulty) across four dimensions in parallel, based on participant mean performance in the previous 12-trial block and normative data from previous studies using REASmash.

1. Number of distractors

Regulated by:

Error rate from the preceding block.

Adjustment rules:

The multiplicative factor m enhances adaptation of multiple dimensions (i.e., number of distractors, cue salience and stimuli presentation time). The starting value is set at 3.0 and decreases by a decrement of 0.3 per block, until reaching a lower bound of 1.0.

- Error rate < 25% → increase by 1 distractor * m
- $25\% \leq \text{Error rate} < 50\%$ → decrease by 1 distractor * m
- Error rate $\geq 50\%$ → decrease by 2 distractors * m

The m factor is retained across sessions, meaning that the multiplier value continues from the previous session when a participant resumes the task in a new session.

Distractor introduction logic:

- The task starts with only the target.

- High-salience (blue) distractors are added first.
- Low-salience (red) distractors are introduced only after 40% of visible molehills are occupied by high-salience distractors.

2. Cue salience

Regulated by:

Error rates from the preceding block.

Cue types:

Cue salience was implemented as a normalized continuous parameter ranging from 0 to 100%, with specific cue types assigned to predefined values or value ranges within this interval. The mapping between cue salience and cue type was defined as follows.

- Red directional arrow appearing at the center of the playing field and pointing to the target corresponds to 100% of cue salience.
- Pulsating target mole (size oscillation) corresponds to a cue salience between 64% and 99%.
- Auditory cue from the target side corresponds to a cue salience between 34% and 63%.
- No cue.

Cue salience values were defined to reflect distinct functional levels of external guidance. The directional arrow was assigned a fixed salience of 100% to represent the highest and unambiguous level of external guidance,

Chapter 5

whereas the other cue types were associated with salience ranges to allow graded modulation within each functional level.

Adjustment rules:

Cue salience adjustments were scaled by the inverse of the cue increment factor, such that larger values of this parameter resulted in more gradual changes in salience across consecutive blocks. Specifically, salience increments increased proportionally with the number of consecutive blocks within the same error-rate range, but were attenuated by the cue increment factor to prevent abrupt adaptations.

- If Error rate $< 25\%$ $\rightarrow$ cue salience % value decreases by (cue increment factor⁻¹) * m
- If $25\% \leq$ Error rate $< 50\%$ $\rightarrow$ cue salience % value increases by (cue increment factor⁻¹) * m
- If Error rate $\geq 50\%$ $\rightarrow$ cue salience % value increases by a fixed full increment (not scaled by m), ensuring a jump to the next cue level.

The cue increment factor was empirically set to 2, meaning that cue salience only changes after 2 consecutive blocks within the same error rate range.

Cues are displayed 2 seconds after the target onset.

3. Active playing field

Regulated by:

The spatial distribution of omissions in the previous 2 blocks.

Adaptation logic:

The active playing field decrement factor was set at 40%, which means that each omission occurring in the outermost active molehill of a given row or column reduces an internal counter by 40% molehill units. When this cumulative reduction exceeds one full unit (i.e., after three such omissions), the corresponding molehill is removed from the active playing field. The active playing field can range to a maximum of 24 molehills distributed across the entire 6 x 4 grid.

4. **Stimuli presentation time**

Regulated by:

Omission rate from the preceding block.

Formula: New presentation time = Previous presentation time + $Kp * (0.75 - (1 - \text{Omission rate in previous block})) * m$

The Kp is a proportionality constant that controls how strongly the stimuli presentation time is adjusted based on the omission rate. It is set to 35 in the current configuration, based on empirical tuning after several pilot testing iterations.

Minimum stimuli presentation time was determined based on performances of 15 healthy controls tested with the classical (evaluative) version of non-immersive REASmash.

Minimum stimuli presentation time setting

These values served as lower bounds for stimuli presentation time adjustments in the auto-adaptive version, ensuring sufficient time for target identification under varying distractor loads.

The classical version of REASmash comprises seven standard levels presenting 24 molehills, displayed on a 6 x 4 playing field grid, and with the target emerging once from each molehill per game level. In level 1, only the

Chapter 5

target is presented (once from each molehill). Levels 2 to 4 present the target with an increasing number of blue-helmet distractors. In levels 5 to 7, the total number of stimuli on the playing field is matched to that of levels 2 to 4 (i.e., 12, 18, and 24 respectively), but with the target and 6, 9, and 12 red-helmet stimuli creating reduced target-distractor salience differences and increasing distractor inhibition demands. The remaining distractors wear the same blue helmets as in the high-salience target-distractor condition.

Previous studies showed that REASmash replicates FIT. Blue distractors (high target-distractor salience) elicit a pop-out effect with no interaction between distractor number and response time. Red distractors (low target-distractor salience) require serial search and active inhibition, with higher distractor counts progressively increasing cognitive load through inhibition demands, causing increased response time.

To determine the minimum stimuli duration in the auto-adaptive version, we focused on levels 5 to 7 of the classical REASmash.

Data analysis on the assessment module outcomes was conducted using an 18-molehills playing field configuration (i.e., excluding trials with target in distal positions, see Figure 1). This setup best reflects the average active playing field observed in pilot auto-adaptive data from post-stroke participants.

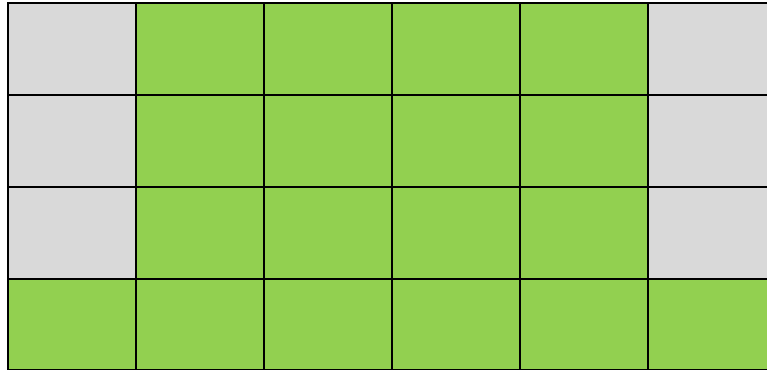


Figure 1. The 18 vs. 24 playing fields. The figure illustrates the 6×4 playing field grid corresponding to the classic REAsmash configuration. The green cells represent the 18-molehills configuration used for response time analysis; grey cells correspond to excluded distal positions.

We observed, consistent with findings reported in the literature²⁸⁸, that the increase in response time remained stable with the addition of three red distractors (i.e., from 5 to 8 to 11), indicating a linear trend. The average cognitive cost, in terms of additional response time, was estimated at 0.27 seconds for three red distractors (i.e., 0.09 seconds per distractor).

Our aim was to determine the minimum stimuli presentation time that would allow participants to respond correctly in 75% of trials. To do so, we used the 75th percentile response time at the 5-red-distractor level as a reference and estimated presentation times for conditions with 1 to 10 red distractors by adding or subtracting the cognitive cost per distractor (Table 1).

Chapter 5

Table 1. Minimum stimuli presentation time (in seconds) as a function of the number of red distractors per trial.

Number of red distractors per trial	Minimum stimuli presentation time (in seconds)
1 red distractor	1.2
2 red distractors	1.3
3 red distractors	1.4
4 red distractors	1.5
5 red distractors	1.6
6 red distractors	1.7
7 red distractors	1.8
8 red distractors	1.8
9 red distractors	1.9
10 red distractors	2.0

Extended material 2

Composite Difficulty Index

The Composite Difficulty Index quantifies trial complexity by jointly considering the three most relevant dimensions of task demand: the stimuli presentation time, the number of red distractors and the number of molehills.

Time normalization (T_norm)

The observed stimuli presentation time per trial (T) was normalized between the dynamic minimum (T_min) and a fixed upper bound (T_max) of 10 s, according to: $T_{\text{norm}} = (T_{\text{max}} - T) / (T_{\text{max}} - T_{\text{min}}(n_{\text{red}}))$, with $T_{\text{max}} = 10$.

In this formulation, T_min represents the minimum stimuli presentation duration parametrically linked to the number of red distractors, reflecting the lower bound derived from normative data.

This normalization ensures that shorter presentation times (relative to their feasible minimum) correspond to higher difficulty values (approaching 1), whereas longer durations approach 0.

Red distractor normalization (R_norm)

The number of red distractors (R) was normalized to the theoretical maximum of 23: $R_{\text{norm}} = R / 23$, clipped to [0,1].

Chapter 5

Molehill normalization (M_norm)

The number of molehills (M) was normalized to the observed range (8-24):
 $M_{\text{norm}} = (M - 8) / (24 - 8)$, clipped to [0,1].

Composite Difficulty Index calculation

The overall index was computed as the mean of the three normalized components, assigning equal weight to visual distractor load, temporal constraints, and spatial complexity.

Extended material 3

Results of the gold-standard assessments

ID	MoCA	BT Time	BT Om	BT First Column	BT Om Left-Right	BHT Time	BHT Errors	BHT Omissions	Go/No-Go RT	Go/No-Go Errors	Go/No-Go omissions
GS1	25	210	4	1	0	127	0	2	635	0	1
GS2	28	263	1	1	-1	220	0	19	455	1	0
GS3	24	330	2	7	2	180	0	6	375	0	6
GS4	26	157	1	1	-1	130	0	0	384	1	0
GS5	27	184	0	1	0	109	2	4	398	0	0
GS6	24	105	0	1	0	83	0	7	401	3	0
GS7	28	178	0	0	0	178	0	0	516	0	0
GS8	24	168	3	1	-3	123	0	3	401	2	0
GS9	26	274	2	0	0	220	0	0	481	3	0
GS10	25	330	0	0	-3	180	0	6	434	2	7

ID	Neg1 RT Left	Neg1 Om Left	Neg1 RT Right	Neg1 Om Right	Neg2 RT Left	Neg2 Om Left	Neg2 RT Right	Neg2 Om Right	VF RT Left	VF Om Left	VF RT Right	VF Om Right
GS1	743	0	763	4	669	1	843	0	645	0	690	0
GS2	1225	18	794	8	1200	15	610	3	1044	6	587	0
GS3	1524	9	1333	2	1229	8	1229	3	746	15	1019	15
GS4	524	0	572	0	459	0	482	0	661	0	672	0
GS5	410	0	451	0	417	0	410	0	471	0	453	0
GS6	516	3	666	1	492	1	452	4	436	0	549	0
GS7	736	0	704	0	857	1	916	1	544	0	548	0
GS8	524	0	533	1	453	1	483	1	569	0	561	0
GS9	521	1	491	1	486	0	616	0	414	0	491	0
GS10	833	0	555	0	686	0	540	0	726	0	685	0

Chapter 5

MoCA = Montreal Cognitive Assessment⁴⁶; BT = Bells Test³⁰; Om = Omission count; BHT = Broken Hearts Test³¹; RT = Reaction Time; Go/No-Go = Go/No-Go (TAP subtest¹³¹); Neg1 = Visual Field - Neglect (TAP subtest); Neg2 = Visual Field -Neglect with Central Task (TAP subtest); VF = Visual Field - Short Version (TAP subtest).

This table was reformatted from the version included in the submitted manuscript for thesis formatting purposes (split into two sections to improve readability). No content or values were modified.

Chapter 6

General Discussion

Reframing assessment in VR: from tasks to systems

The use of VR SG in clinical practice challenges how behavioral assessment is typically conceived. The present thesis does not aim to introduce a new modular tool per se, but rather to position assessment within a framework where outcome parameters emerge from interactions between task structure, technological capabilities, and measurement methods.

A central point that emerged from this thesis is that increasing technological complexity does not automatically improve assessment. Increasing environmental complexity, for example through realistic immersive VR environments or the integration of technologies such as eye tracking, has limited value if the resulting behavioral data cannot be interpreted within a rigorous and theory-driven framework. Without adapted metrics and theoretically grounded paradigms, VR risks creating ‘technologically sophisticated but methodologically limited’ innovations in diagnosis and neurorehabilitation. The first challenge of this thesis was therefore to align technological implementation with structured cognitive frameworks and measurement strategies that preserve interpretability.

This doctoral thesis used the REAsmash SG paradigm, developed during the PhDs of Gauthier Everard and Khawla Ajana from our research team^{219,261,289–291}. The overarching objective was to address limitations in the assessment and rehabilitation of post-stroke attentional deficits by extending an existing theory-driven VR SG paradigm into a broader assessment and rehabilitation framework to enable more precise, quantitative, and adaptive investigation of cognitive processes.

Chapter 6 - General Discussion

Four interrelated objectives were pursued (Chapter 1). The first was to extend the REAsmash paradigm to improve the characterization of spatial attention and distractor inhibition (Chapters 2-5). In Chapter 2, the non-immersive implementation demonstrated sensitivity to both group-level differences and task-dependent modulation of performance. Behavioral outcomes varied according to target-distractor salience and distractor number, in line with the theoretical framework underlying REAsmash and with previous findings obtained in immersive VR versions of the paradigm. This contributes to addressing the limited availability of controlled paradigms specifically targeting distractor inhibition. Although distractor inhibition represents a core component of visual attention, it remains rarely isolated and systematically manipulated in applied and VR-based assessment frameworks^{292,293}.

The second objective was to examine how the level of VR immersion influenced cognitive performance. In Chapter 3, immersive and non-immersive modules were compared to assess how interaction modality and environment influenced attentional processing.

The third objective was to refine behavioral characterization through the integration of process-oriented measures. In Chapter 4, this objective was addressed through REAsmash-ET, integrating ET and upper limb kinematics to characterize visual exploration and motor interactions beyond response time and error or omission measures, and providing a deeper understanding of attentional mechanisms.

The fourth objective was to extend the assessment framework using theory-driven DDA to enable continuous and multi-variable adaptation of task demands derived from individual performance and relative to normative values. The framework presented in Chapter 5 allowed the simultaneous manipulation of multiple attentional components providing personalized and scalable neurorehabilitation.

Collectively, these objectives demonstrate progression from the extension of an existing experimental paradigm to the development of integrated and

adaptive tools for assessment and rehabilitation. By bridging theoretical foundations, methodological innovation, and translational application, this thesis aimed to promote a more precise, dynamic, and functionally relevant approach to cognitive assessment and rehabilitation after stroke. In this General Discussion, I discuss each of the objectives relative to the research findings presented in this thesis.

Stability of paradigms and the role of immersion (Chapters 2 and 3)

This thesis demonstrates that basing VR SG on a structured paradigm grounded in cognitive theory (such as FIT) ensures stability of performance across different VR configurations (Chapters 2-4). This stability enables direct comparison between non-immersive and immersive implementations, allowing the isolation of technological effects on performance (Chapter 3). In Chapter 3, the REAsmash paradigm was evaluated using non-immersive and immersive VR in post-stroke participants and healthy controls, with VR sessions administered within one week of each other. Although immersive VR increased response times, the FIT-based diagnostic pattern was preserved, demonstrating transferability across VR configurations.

In the broader literature, immersion effects are often inferred from studies employing different tasks, devices, and outcome measures, introducing methodological heterogeneity that limits the interpretability of these findings⁵⁹. By comparing the same paradigm within the same participants under controlled conditions, the present study minimizes variability related to task structure and population, allowing the specific contribution of immersion to be more directly assessed.

From a clinical perspective, these data from Chapter 3 imply that the choice of VR environment and the degree of immersion must be considered alongside the task itself, as it directly shapes task demands and performance. These same principles extend to SG designed for rehabilitation, where technological configurations may directly impact engagement and overall cognitive load. From our results, we may suggest that non-immersive VR

Chapter 6 - General Discussion

could be preferentially used in early or more cognitively demanding stages of rehabilitation, as it allows targeting the cognitive functions probed by the paradigm while limiting additional demands related to VR immersion. This may facilitate early detection of distractor inhibition and spatial attention deficits in patients with greater difficulties and support early rehabilitation. Immersive VR may then be introduced to target the same cognitive functions within a more demanding task context, while preserving the underlying paradigm, thereby enabling assessment and training under conditions closer to real-world complexity.

ET in VR: from measurement transfer to methodological adaptation (Chapter 4)

A paradigmatic example of approaches that risk ‘technological sophistication and methodological limitation’ is represented by VR SG that attempt to integrate ET metrics without adapting them to the immersive VR setting. Classical ET approaches rely on fixed spatial references, stable eye-to-stimulus distances, and constrained head position. These assumptions do not hold in immersive VR, where stimuli are distributed in three-dimensional space and the participant continuously changes position. In this framework, and with specific regard to fixation measures, the key issue is to define algorithms that allow a meaningful interpretation of gaze behavior in relation to task demands.

In the present thesis (Chapter 4), ET fixations were explicitly treated within the task context as markers of cognitive interactions with stimuli, rather than as purely spatial events. The I-DT algorithmic approach was adapted to this functional interpretation and modulated to account for the three-dimensional structure of the task. A major contribution of this thesis lies in extending the I-DT algorithm by incorporating eye-to-stimulus distance ranges, allowing comparable measures across 3D spatial positions. Thresholds were further calibrated to the size of salient stimulus features, enabling the distinction between consecutive interactions with adjacent parts of the same stimulus. This improvement in the I-DT algorithm enabled the identification of reliable behavioral signatures, including inefficient exploration,

perseverative tendencies, and altered updating of information. Importantly, ET metrics indexing distractor inhibition demands were sensitive to the experimental manipulations, showing systematic modulation as a function of target-distractor salience and distractor number. In particular, cumulative fixation time on distractors increased with lower target-distractor salience and higher distractor number. Capture fixation number was also modulated by target-distractor salience and distractor number, whereas re-capture fixations remained relatively rare in healthy participants. Age-related differences further emerged in visual search efficiency, with older participants showing longer cumulative fixation times on distractors, supporting the sensitivity of the framework to inter-individual variability in attentional performance.

By explicitly linking ET metrics to task parameters within a theory-driven framework, the present approach supports a more grounded interpretation of visual exploration in relation to attentional mechanisms. REASmash-ET thus addresses key limitations of previous work, in which ET measures are often applied without adaptation to immersive environments or remain insufficiently anchored to task structure, limiting their interpretability in relation to underlying cognitive processes²⁶⁰.

In a clinical context, this approach may support the identification of distinct attentional profiles and enable the objective quantification of how controlled increases in specific cognitive demands (e.g., distractor load or salience) differentially modulate gaze metrics. This, in turn, may allow a more precise characterization of cognitive impairments and better targeting of rehabilitation interventions. The integration of upper limb kinematics further complements this approach by enabling the temporal linking of visual exploration and motor responses, providing additional insight into the coupling between attention and action.

Chapter 6 - General Discussion

From assessment to adaptation: toward dynamic task regulation (Chapter 5)

A central element of this thesis was the development of a DDA algorithm for cognitive rehabilitation based on a stable and theoretically grounded task. DDA-REAsmash adaptive rules were informed by the structured characterization of task demands established in the assessment modules (Chapters 2 and 3) and further supported by process-oriented insights from the ET study (Chapter 4). The algorithm was further constrained by normative values, anchoring adaptation to both individual performance and population-based references.

The results showed that success rates rapidly converged toward the predefined optimal engagement range within a few blocks. Task difficulty trajectories exhibited a consistent pattern of early adjustment followed by stabilization at participant-specific levels, suggesting that the algorithm identified and maintained individualized operating points. Importantly, variations in distractor inhibition demands and spatial configuration were aligned with baseline attentional profiles derived from the REAsmash assessment module and gold-standard assessments, indicating that adaptation was sensitive to task-relevant aspects of attentional performance.

Rather than representing a purely theoretical proposal, the present work provides an operational implementation of a DDA framework and demonstrates its feasibility in regulating task demands in a consistent and interpretable manner. In this sense, DDA-REAsmash addresses a key limitation of previous adaptive approaches, which often rely on performance-based rules without systematically integrating normative references or explicitly modelling the cognitive processes engaged by the task²⁹⁴⁻²⁹⁶.

Structured DDA frameworks grounded in cognitive theory and constrained by normative references may facilitate adaptive rehabilitation approaches in which cognitive and environmental complexity can be progressively increased while preserving objective and interpretable characterization of

the underlying attentional processes. In a clinical context, such approaches may enable individualized rehabilitation strategies in which task demands are continuously adjusted to the performance of each individual, while remaining aligned with the cognitive processes targeted by the intervention, allowing selective modulation of attentional components rather than non-specific difficulty scaling.

Thesis limitations and future perspectives

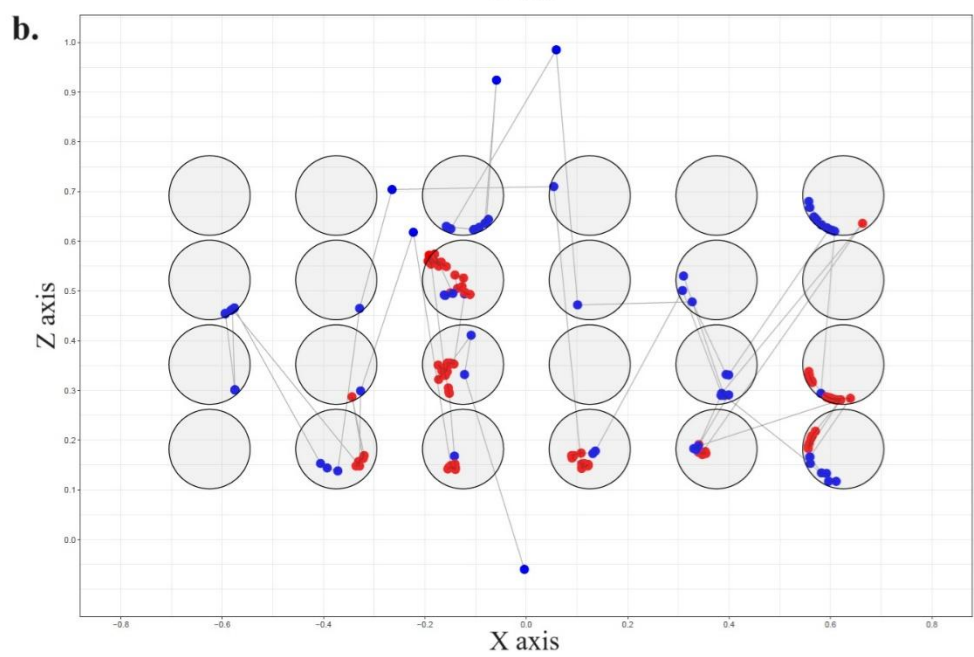
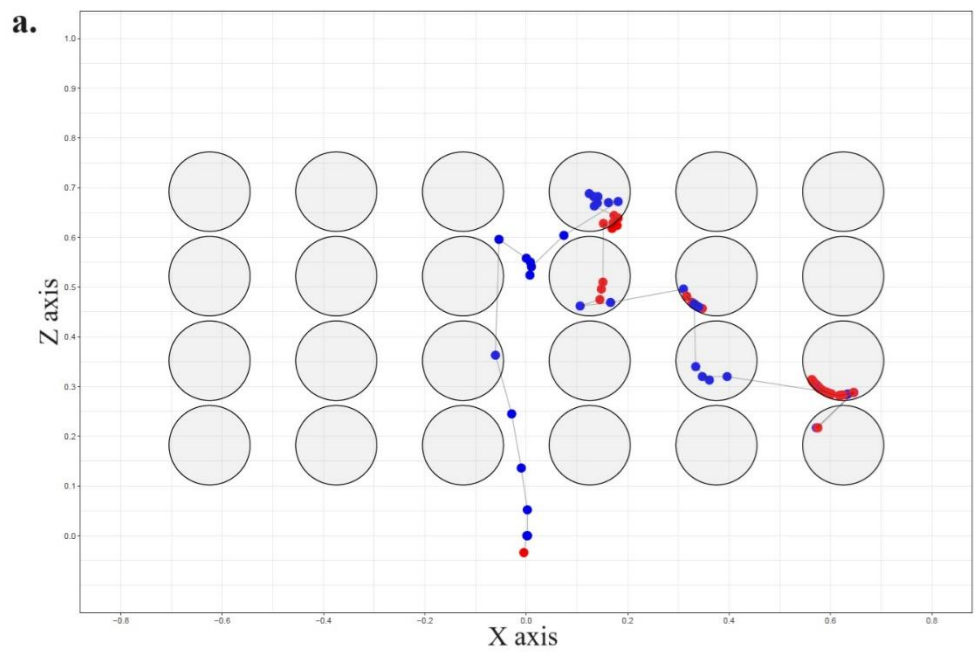
While the present thesis addressed its main objectives and provides meaningful contributions to the scientific literature, it also highlights several areas that warrant further investigation. The limitations of each empirical chapter are presented within the respective studies, and here an integrated summary is provided, together with the main directions for future research emerging from this work.

A first consideration relates to the overall positioning of this work as a methodological and pre-clinical step toward clinical application (Chapters 2-4). The main objective was to develop and test a consistent framework for the assessment of attention through the systematic modulation of attentional processes under controlled conditions. As such, sample sizes, experimental control, and study designs were appropriate to this stage of development, but they limit the generalizability of the findings and the strength of direct clinical inferences. Importantly, however, results across studies were highly consistent, with stable task effects, convergent behavioral patterns, and reproducible process-level metrics, supporting the internal coherence of the proposed framework. Future research should focus on extending this work to larger and more heterogeneous post-stroke populations and on establishing the clinical validity of the assessment modules in relation to standard neuropsychological measures and functional outcomes.

A second limitation relates to the clinical application of process-oriented ET metrics presented in Chapter 4, where only healthy participants were tested. In continuity with the methodological work presented in this thesis, we are currently finalizing a study applying an extended version of the REAsmash-

Chapter 6 - General Discussion

ET framework to stroke survivors. This new research introduces a fully adaptive I-DT algorithm, in which the gaze dispersion threshold is dynamically updated based on real-time eye-to-stimulus relationships. This novelty addresses a key challenge in clinical populations, where variability in posture and interaction conditions can affect gaze data²⁹⁷. In parallel, a temporal analysis framework was implemented to isolate early exploratory orienting and post-target processing. This research was initially intended to be completed within the doctoral period, but recruitment proved more demanding than anticipated. The study was initially conducted as a single-center study and during autumn 2025, we expanded the study to two additional sites to increase the clinical sample. Preliminary data analyses on 11 stroke survivors with confirmed USN compared with 30 age-matched healthy controls indicate that early-stage visual exploration in USN is characterized by a spatially asymmetric distribution of gaze interactions, with a higher number of capture fixations directed toward the ipsilesional hemifield. At the same time, capture fixation rate, defined as the number of repeated fixations per distractor, showed no clear modulation by distractor-inhibition demands and no lateralized effects, and re-capture fixations were rare across conditions (Figure D1). These findings indicate that the increased number of ipsilesional interactions does not reflect perseverative engagement with individual stimuli, but rather a broader distribution of gaze across multiple distractors within the ipsilesional hemifield. The absence of lateralized effects during post-target processing further suggests that USN deficits are primarily expressed at the level of attentional allocation rather than post-target processing. These results support the relevance of process-oriented ET metrics within this framework, showing that they provide interpretable and reliable markers of distinct attentional components and can refine the characterization of cognitive deficits such as spatial and non-spatial (distractor inhibition) impairments beyond conventional outcome measures.



Chapter 6 - General Discussion

Figure D1. Two representative scan paths obtained during a single trial in a stroke survivor with USN (a.) and an age-matched healthy control (b.). The playing field is schematized on the X and Y planes, and each circle corresponds to one of the 24 ROIs, representing the stimuli distributed across the virtual environment. In both examples, the target was located in the rightmost column and in the second row relative to the participant's point of view. Each colored point represents an individual gaze sample. Red points correspond to gaze samples identified by the adaptive I-DT algorithm as belonging to a fixation, whereas blue points correspond to gaze samples associated with saccadic exploration. In the participant with USN, visual exploration was predominantly restricted to the ipsilesional hemifield. Overlapping fixation analyses identified two capture fixations within the ipsilesional hemifield in the USN participant, whereas the healthy control exhibited one capture fixation in each hemifield, reflecting a more spatially distributed exploration pattern despite a similar capture fixation rate at the trial level. In both participants, this trial did not show any re-capture fixations.

Establishing this link between task demands, gaze behavior, and interpretable cognitive patterns in individuals with USN was not only an innovative methodological step, but also a deliberate strategy to support the expansion of the project. By providing structured evidence in 11 participants with confirmed USN, the aim will be to facilitate collaboration with additional centers, allowing the inclusion of larger and more diverse cohorts in future research. This will enable direct comparisons between populations with and without USN, across different stages of recovery, lesion locations, and levels of impairment as defined by standard clinical assessments.

A third limitation relates to the absence of direct evidence regarding clinical efficacy of DDA-REAsmash, where the focus of Chapter 5 was on feasibility and adaptive behavior rather than therapeutic outcomes. While the algorithm demonstrated the ability to dynamically modulate task difficulty and converge toward individualized levels of cognitive demand, its impact on functional recovery remains to be established. Future research should extend this framework to larger and more diverse clinical

populations. A randomized, single-blind, crossover-controlled study is currently envisaged, comparing one month of conventional rehabilitation with one month of conventional rehabilitation supplemented by four weekly sessions of DDA-REAsmash.

Looking ahead, an important direction concerns the extension of the present DDA framework to immersive environments. An immersive version of the DDA-REAsmash has already been conceptualized. This module represents the integration of the methodological and theoretical developments introduced in this doctoral thesis, combining structured task design, process-oriented ET metrics, and dynamic task regulation within a single framework. In this configuration, the algorithm retains the multidimensional structure of the non-immersive implementation while incorporating ET metrics to distinguish between errors and omissions arising from deficient visual exploration and those related to motor execution constraints. This solution was specifically conceived to enable training sessions involving the more affected upper limb. However, the ability of the algorithm to reliably disentangle motor and cognitive components remains to be formally evaluated.

Conclusion

This thesis shows that VR-based assessment is not a simple extension of existing methods, but a shift toward integrated systems in which task design, technological environment, and measurement tools are tightly interconnected. By combining stable task paradigms, controlled manipulation of immersion, adapted ET methodologies, and dynamic task regulation, this research contributes to a more rigorous and interpretable integrated framework for VR-based assessment and neurorehabilitation of attentional impairments.

List of Abbreviations

AD - Angular Dispersion
ADLs - Activities of Daily Living
ANOVA - Analysis of Variance
ARAT - Action Research Arm Test
BBT - Box and Block Test
CAVE - Cave Automatic Virtual Environment
CDI - Composite Difficulty Index
CT - Computed Tomography
d - Distance between the eyes and the stimuli
DALYs - Disability-Adjusted Life Years
DDA - Dynamic Difficulty Adjustment
ET - Eye-Tracking
FIT - Feature-Integration Theory
FMA - Fugl-Meyer Assessment
FOV - Field of View
HMD - Head-Mounted Display
ICF - International Classification of Functioning, Disability and Health
I-DT - Identification by Dispersion Threshold
iVR - Immersive Virtual Reality
LD - Linear Dispersion
LPS - Large Projection System
MMSE - Mini-Mental State Examination
MoCA - Montreal Cognitive Assessment
MRI - Magnetic Resonance Imaging
niVR - Non-Immersive Virtual Reality
OCS - Oxford Cognitive Screen
ROI - Region of Interest
RRT - Relative Response Time
RT - Response Time

Chapter 6 - General Discussion

SG - Serious Game

SPARC - Spectral Arc Length

STROBE - Strengthening the Reporting of Observational Studies in Epidemiology

TAP - Test for Attentional Performance

TIDieR - Template for Intervention Description and Replication

UL - Upper Limb

USN - Unilateral Spatial Neglect

VR - Virtual Reality

XR - Extended Reality

Bibliography

1. Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2197-2223. doi:10.1016/S0140-6736(12)61689-4
2. Phipps MS, Cronin CA. Management of acute ischemic stroke. *BMJ*. 2020;368:l6983. doi:10.1136/bmj.l6983
3. Pu L, Wang L, Zhang R, Zhao T, Jiang Y, Han L. Projected Global Trends in Ischemic Stroke Incidence, Deaths and Disability-Adjusted Life Years From 2020 to 2030. *Stroke*. 2023;54(5):1330-1339. doi:10.1161/STROKEAHA.122.040073
4. Fan J, Li X, Yu X, et al. Global Burden, Risk Factor Analysis, and Prediction Study of Ischemic Stroke, 1990–2030. *Neurology*. 2023;101(2):e137-e150. doi:10.1212/WNL.0000000000207387
5. Cramer SC. Repairing the human brain after stroke: I. Mechanisms of spontaneous recovery. *Ann Neurol*. 2008;63(3):272-287. doi:10.1002/ana.21393
6. Kwakkel G, Kollen B, Lindeman E. Understanding the pattern of functional recovery after stroke: facts and theories. *Restor Neurol Neurosci*. 2004;22(3-5):281-299.
7. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet*. 2011;377(9778):1693-1702. doi:10.1016/S0140-6736(11)60325-5
8. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. 2016;47(6):e98-e169. doi:10.1161/STR.0000000000000098

References

9. Li X, He Y, Wang D, Rezaei MJ. Stroke rehabilitation: from diagnosis to therapy. *Front Neurol*. 2024;15. doi:10.3389/fneur.2024.1402729
10. Egan M, Kessler D, Gurgel-Juarez N, et al. Stroke rehabilitation adaptive approaches: A theory-focused scoping review. *Scand J Occup Ther*. 2024;31(1):1-13. doi:10.1080/11038128.2023.2257228
11. Shahid J, Kashif A, Shahid MK. A Comprehensive Review of Physical Therapy Interventions for Stroke Rehabilitation: Impairment-Based Approaches and Functional Goals. *Brain Sci*. 2023;13(5):717. doi:10.3390/brainsci13050717
12. Kwakkel G, Stinear C, Essers B, et al. Motor rehabilitation after stroke: European Stroke Organisation (ESO) consensus-based definition and guiding framework. *European Stroke Journal*. 2023;8(4):880-894. doi:10.1177/23969873231191304
13. Jokinen H, Melkas S, Ylikoski R, et al. Post-stroke cognitive impairment is common even after successful clinical recovery. *Eur J Neurol*. 2015;22(9):1288-1294. doi:10.1111/ene.12743
14. Tabone F, Stockley RC, Demeyere N. Why cognition matters: perspectives in post-stroke motor rehabilitation research. *Disability and Rehabilitation*. 2026;0(0):1-7. doi:10.1080/09638288.2026.2652832
15. Draheim C, Pak R, Draheim AA, Engle RW. The role of attention control in complex real-world tasks. *Psychon Bull Rev*. 2022;29(4):1143-1197. doi:10.3758/s13423-021-02052-2
16. Stolwyk RJ, Mihaljcic T, Wong DK, Chapman JE, Rogers JM. Poststroke Cognitive Impairment Negatively Impacts Activity and Participation Outcomes. *Stroke*. 2021;52(2):748-760. doi:10.1161/STROKEAHA.120.032215
17. Stiekema APM, Nijse B, de Kort PLM, Spikman JM, Visser-Meily JMA, van Heugten CM. The relationship between social cognition and participation in the long term after stroke. *Neuropsychological Rehabilitation*. 2021;31(2):278-292. doi:10.1080/09602011.2019.1692670

18. VanGilder JL, Hooyman A, Peterson DS, Schaefer SY. Post-stroke cognitive impairments and responsiveness to motor rehabilitation: A review. *Curr Phys Med Rehabil Rep*. 2020;8(4):461-468. doi:10.1007/s40141-020-00283-3
19. McMahon D, Micallef C, Quinn TJ. Review of clinical practice guidelines relating to cognitive assessment in stroke. *Disabil Rehabil*. 2022;44(24):7632-7640. doi:10.1080/09638288.2021.1980122
20. Esposito E, Shekhtman G, Chen P. Prevalence of spatial neglect post-stroke: A systematic review. *Ann Phys Rehabil Med*. 2021;64(5):101459. doi:10.1016/j.rehab.2020.10.010
21. Heilman K, Valenstein E, Watson R. Neglect and Related Disorders. *Semin Neurol*. 1984;4(02):209-219. doi:10.1055/s-2008-1041551
22. Williams LJ, Kernot J, Hillier SL, Loetscher T. Spatial Neglect Subtypes, Definitions and Assessment Tools: A Scoping Review. *Front Neurol*. 2021;12. doi:10.3389/fneur.2021.742365
23. Punt TD, Riddoch MJ, Humphreys GW. Motor extinction: a deficit of attention or intention? *Front Hum Neurosci*. 2013;7:644. doi:10.3389/fnhum.2013.00644
24. Bisiach E, Luzzatti C. Unilateral neglect of representational space. *Cortex*. 1978;14(1):129-133. doi:10.1016/s0010-9452(78)80016-1
25. Bartolomeo P. Visual and motor neglect: Clinical and neurocognitive aspects. *Revue Neurologique*. 2021;177(6):619-626. doi:10.1016/j.neurol.2020.09.003
26. Posner MI, Petersen SE. The attention system of the human brain. *Annu Rev Neurosci*. 1990;13:25-42. doi:10.1146/annurev.ne.13.030190.000325
27. Petersen SE, Posner MI. The attention system of the human brain: 20 years after. *Annu Rev Neurosci*. 2012;35:73-89. doi:10.1146/annurev-neuro-062111-150525
28. Corbetta M, Shulman GL. Spatial neglect and attention networks. *Annu Rev Neurosci*. 2011;34:569-599. doi:10.1146/annurev-neuro-061010-113731

References

29. Lunven M, Bartolomeo P. Attention and spatial cognition: Neural and anatomical substrates of visual neglect. *Annals of Physical and Rehabilitation Medicine*. 2017;60(3):124-129. doi:10.1016/j.rehab.2016.01.004
30. Gauthier L, Dehaut F, Joanette Y. The Bells Test: A quantitative and qualitative test for visual neglect. *International Journal of Clinical Neuropsychology*. 1989;11:49-54.
31. Demeyere N, Riddoch MJ, Slavkova ED, Bickerton WL, Humphreys GW. The Oxford Cognitive Screen (OCS): validation of a stroke-specific short cognitive screening tool. *Psychol Assess*. 2015;27(3):883-894. doi:10.1037/pas0000082
32. Schenkenberg T, Bradford DC, Ajax ET. Line bisection and unilateral visual neglect in patients with neurologic impairment. *Neurology*. 1980;30(5):509-517. doi:10.1212/wnl.30.5.509
33. Howieson D. Current limitations of neuropsychological tests and assessment procedures. *Clin Neuropsychol*. 2019;33(2):200-208. doi:10.1080/13854046.2018.1552762
34. Giannakou I, Lin D, Punt D. Computer-based assessment of unilateral spatial neglect: A systematic review. *Front Neurosci*. 2022;16:912626. doi:10.3389/fnins.2022.912626
35. Guilbert A. Clinical assessment of unilateral spatial neglect dissociations and heterogeneities: A narrative synthesis. *Neuropsychology*. 2023;37(4):450-462. doi:10.1037/neu0000841
36. Terruzzi S, Albini F, Massetti G, Etzi R, Gallace A, Vallar G. The Neuropsychological Assessment of Unilateral Spatial Neglect Through Computerized and Virtual Reality Tools: A Scoping Review. *Neuropsychol Rev*. 2024;34(2):363-401. doi:10.1007/s11065-023-09586-3
37. Moran R, Zehetleitner M, Liesefeld HR, Müller HJ, Usher M. Serial vs. parallel models of attention in visual search: accounting for benchmark RT-distributions. *Psychon Bull Rev*. 2016;23(5):1300-1315. doi:10.3758/s13423-015-0978-1

38. Yantz CJ, McCaffrey RJ. Social facilitation effect of examiner attention or inattention to computer-administered neuropsychological tests: first sign that the examiner may affect results. *Clin Neuropsychol*. 2007;21(4):663-671. doi:10.1080/13854040600788158
39. Erez ABH, Katz N, Ring H, Soroker N. Assessment of spatial neglect using computerised feature and conjunction visual search tasks. *Neuropsychol Rehabil*. 2009;19(5):677-695. doi:10.1080/09602010802711160
40. Treisman AM, Gelade G. A feature-integration theory of attention. *Cognitive Psychology*. 1980;12(1):97-136. doi:10.1016/0010-0285(80)90005-5
41. Lustig C, Hasher L, Zacks RT. Inhibitory deficit theory: Recent developments in a "new view." In: *Inhibition in Cognition*. American Psychological Association; 2007:145-162. doi:10.1037/11587-008
42. Stefani M, Sauter M. Relative contributions of oculomotor capture and disengagement to distractor-related dwell times in visual search. *Sci Rep*. 2023;13(1):16676. doi:10.1038/s41598-023-43604-x
43. Puig-Pijoan A, Giralt-Steinhauer E, Zabalza de Torres A, et al. Underdiagnosis of Unilateral Spatial Neglect in stroke unit. *Acta Neurol Scand*. 2018;138(5):441-446. doi:10.1111/ane.12998
44. Sun JH, Tan L, Yu JT. Post-stroke cognitive impairment: epidemiology, mechanisms and management. *Ann Transl Med*. 2014;2(8):80. doi:10.3978/j.issn.2305-5839.2014.08.05
45. Rai GS. The Mini-Mental State Examination. *J Am Geriatr Soc*. 1993;41(3):346. doi:10.1111/j.1532-5415.1993.tb06721.x
46. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53(4):695-699. doi:10.1111/j.1532-5415.2005.53221.x

References

47. Einstad MS, Saltvedt I, Lydersen S, et al. Associations between post-stroke motor and cognitive function: a cross-sectional study. *BMC Geriatr.* 2021;21(1):103. doi:10.1186/s12877-021-02055-7
48. Montero-Odasso M, Almeida QJ, Bherer L, et al. Consensus on Shared Measures of Mobility and Cognition: From the Canadian Consortium on Neurodegeneration in Aging (CCNA). *The Journals of Gerontology: Series A.* 2019;74(6):897-909. doi:10.1093/gerona/gly148
49. Hazelton C, McGill K, Campbell P, et al. Perceptual Disorders After Stroke: A Scoping Review of Interventions. *Stroke.* 2022;53(5):1772-1787. doi:10.1161/STROKEAHA.121.035671
50. Gentsch A, Weber A, Synofzik M, Vosgerau G, Schütz-Bosbach S. Towards a common framework of grounded action cognition: Relating motor control, perception and cognition. *Cognition.* 2016;146:81-89. doi:10.1016/j.cognition.2015.09.010
51. Michael D. *Serious Games: Games That Educate, Train and Inform.* Thomson Course Technology; 2006.
52. Bergeron BP. *Developing Serious Games.* Hingham, Mass: Charles River Media; c2006. ISBN:1584504447. c2006.
53. Smith SP, Blackmore K, Nesbitt K. A Meta-Analysis of Data Collection in Serious Games Research. In: Loh CS, Sheng Y, Ifenthaler D, eds. *Serious Games Analytics: Methodologies for Performance Measurement, Assessment, and Improvement.* Springer International Publishing; 2015:31-55. doi:10.1007/978-3-319-05834-4_2
54. Tong T, Chignell M, Tierney MC, Lee J. A Serious Game for Clinical Assessment of Cognitive Status: Validation Study. *JMIR Serious Games.* 2016;4(1):e7. doi:10.2196/games.5006
55. Parsons TD. Virtual Reality for Enhanced Ecological Validity and Experimental Control in the Clinical, Affective and Social Neurosciences. *Front Hum Neurosci.* 2015;9:660. doi:10.3389/fnhum.2015.00660

56. Wohlgenannt I, Simons A, Stieglitz S. Virtual Reality. *Bus Inf Syst Eng.* 2020;62(5):455-461. doi:10.1007/s12599-020-00658-9
57. Ventura S, Brivio E, Riva G, Baños RM. Immersive Versus Non-immersive Experience: Exploring the Feasibility of Memory Assessment Through 360° Technology. *Front Psychol.* 2019;10:2509. doi:10.3389/fpsyg.2019.02509
58. Neguț A, Matu SA, Sava FA, David D. Virtual reality measures in neuropsychological assessment: a meta-analytic review. *Clin Neuropsychol.* 2016;30(2):165-184. doi:10.1080/13854046.2016.1144793
59. Demeco A, Zola L, Frizziero A, et al. Immersive Virtual Reality in Post-Stroke Rehabilitation: A Systematic Review. *Sensors (Basel).* 2023;23(3):1712. doi:10.3390/s23031712
60. Laver KE, Lange B, George S, et al. Virtual reality for stroke rehabilitation - Laver, KE - 2025 | Cochrane Library. Accessed April 15, 2026. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008349.pub5/full>
61. Gómez Bergin AD, Craven MP. Virtual, augmented, mixed, and extended reality interventions in healthcare: a systematic review of health economic evaluations and cost-effectiveness. *BMC Digit Health.* 2023;1(1):53. doi:10.1186/s44247-023-00054-9
62. Cano-de-la-Cuerda R, Blázquez-Fernández A, Marcos-Antón S, et al. Economic Cost of Rehabilitation with Robotic and Virtual Reality Systems in People with Neurological Disorders: A Systematic Review. *Journal of Clinical Medicine.* 2024;13(6):6. doi:10.3390/jcm13061531
63. Saldana D, Neureither M, Schmiesing A, et al. Applications of Head-Mounted Displays for Virtual Reality in Adult Physical Rehabilitation: A Scoping Review. *Am J Occup Ther.* 2020;74(5):7405205060p1-7405205060p15. doi:10.5014/ajot.2020.041442
64. Adeghe E, Okolo C, Ojeyinka O. A review of the integration of virtual reality in healthcare: implications for patient education and treatment outcomes.

References

- International Journal of Science and Technology Research Archive*. Published online April 24, 2024;79-088. doi:10.53771/ijstra.2024.6.1.0032
65. Tao L, Wang Q, Liu D, Wang J, Zhu Z, Feng L. Eye tracking metrics to screen and assess cognitive impairment in patients with neurological disorders. *Neurol Sci*. 2020;41(7):1697-1704. doi:10.1007/s10072-020-04310-y
 66. Holmqvist K, Nyström M, Andersson R, Dewhurst R, Jarodzka H, Van de Weijer J. *Eye Tracking: A Comprehensive Guide to Methods and Measures*. Oxford University Press; 2011. Accessed January 15, 2025. <https://global.oup.com/academic/product/eye-tracking-9780199697083?cc=nl&lang=en&>
 67. Carter BT, Luke SG. Best practices in eye tracking research. *International Journal of Psychophysiology*. 2020;155:49-62. doi:10.1016/j.ijpsycho.2020.05.010
 68. Kaufmann BC, Knobel SEJ, Nef T, Müri RM, Cazzoli D, Nyffeler T. Visual Exploration Area in Neglect: A New Analysis Method for Video-Oculography Data Based on Foveal Vision. *Front Neurosci*. 2019;13:1412. doi:10.3389/fnins.2019.01412
 69. Kaufmann BC, Cazzoli D, Koenig-Bruhin M, Müri RM, Nef T, Nyffeler T. Video-Oculography During Free Visual Exploration to Detect Right Spatial Neglect in Left-Hemispheric Stroke Patients With Aphasia: A Feasibility Study. *Front Neurosci*. 2021;15:640049. doi:10.3389/fnins.2021.640049
 70. Khan A, Imam YZ, Muneer M, Al Jerdi S, Gill SK. Virtual reality in stroke recovery: a meta-review of systematic reviews. *Bioelectronic Medicine*. 2024;10(1):23. doi:10.1186/s42234-024-00150-9
 71. Bowen A, Hazelton C, Pollock A, Lincoln NB. Cognitive rehabilitation for spatial neglect following stroke. *Cochrane Database Syst Rev*. 2013;2013(7):CD003586. doi:10.1002/14651858.CD003586.pub3

72. Redding GM, Rossetti Y, Wallace B. Applications of prism adaptation: a tutorial in theory and method. *Neurosci Biobehav Rev*. 2005;29(3):431-444. doi:10.1016/j.neubiorev.2004.12.004
73. Rossetti Y, Rode G, Pisella L, et al. Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature*. 1998;395(6698):166-169. doi:10.1038/25988
74. Serino A, Angeli V, Frassinetti F, Làdavas E. Mechanisms underlying neglect recovery after prism adaptation. *Neuropsychologia*. 2006;44(7):1068-1078. doi:10.1016/j.neuropsychologia.2005.10.024
75. Rode G, Klos T, Courtois-Jacquin S, Rossetti Y, Pisella L. Neglect and prism adaptation: a new therapeutic tool for spatial cognition disorders. *Restor Neurol Neurosci*. 2006;24(4-6):347-356.
76. P C, K H, C M, A S, Ga E. Does prism adaptation treatment reduce spatial neglect and improve function? *Frontiers in rehabilitation sciences*. 2025;6. doi:10.3389/fresc.2025.1539887
77. Culicetto L, Giustiniani A, Lo Buono V, et al. From real to virtual prism adaptation therapy: a systematic review on benefits and challenges of a new potential rehabilitation approach. *Front Psychol*. 2024;15. doi:10.3389/fpsyg.2024.1391711
78. Naito Y, Koshino Y, Ota H, et al. Short-term effect of prism adaptation treatment on severity of unilateral spatial neglect following right hemispheric stroke: a systematic review and meta-analysis. *J Rehabil Med*. 2025;57:jrm42542. doi:10.2340/jrm.v57.42542
79. Carter AR, Barrett AM. Recent advances in treatment of spatial neglect: networks and neuropsychology. *Expert Rev Neurother*. 2023;23(7):587-601. doi:10.1080/14737175.2023.2221788
80. Kerkhoff G, Schenk T. Rehabilitation of neglect: an update. *Neuropsychologia*. 2012;50(6):1072-1079. doi:10.1016/j.neuropsychologia.2012.01.024

References

81. Carter AR, Barrett AM. Recent advances in treatment of spatial neglect: networks and neuropsychology. *Expert Rev Neurother.* 2023;23(7):587-601. doi:10.1080/14737175.2023.2221788
82. Robertson IH, North N. Spatio-motor cueing in unilateral left neglect: the role of hemispace, hand and motor activation. *Neuropsychologia.* 1992;30(6):553-563. doi:10.1016/0028-3932(92)90058-t
83. Kerkhoff G. Rehabilitation of Visuospatial Cognition and Visual Exploration in Neglect: a Cross-over Study. *Restor Neurol Neurosci.* 1998;12(1):27-40.
84. Kashiwagi FT, El Dib R, Gomaa H, et al. Noninvasive Brain Stimulations for Unilateral Spatial Neglect after Stroke: A Systematic Review and Meta-Analysis of Randomized and Nonrandomized Controlled Trials. *Neural Plast.* 2018;2018:1638763. doi:10.1155/2018/1638763
85. Umeonwuka C, Roos R, Ntsiea V. Current trends in the treatment of patients with post-stroke unilateral spatial neglect: a scoping review. *Disabil Rehabil.* 2022;44(11):2158-2185. doi:10.1080/09638288.2020.1824026
86. Salatino A, Zavattaro C, Gammeri R, et al. Virtual reality rehabilitation for unilateral spatial neglect: A systematic review of immersive, semi-immersive and non-immersive techniques. *Neurosci Biobehav Rev.* 2023;152:105248. doi:10.1016/j.neubiorev.2023.105248
87. Gouret A, Le Bars S, Porssut T, Waszak F, Chokron S. Advancements in brain-computer interfaces for the rehabilitation of unilateral spatial neglect: a concise review. *Front Neurosci.* 2024;18. doi:10.3389/fnins.2024.1373377
88. Hocine N, Gouaïch A, Cerri SA, Mottet D, Froger J, Laffont I. Adaptation in serious games for upper-limb rehabilitation: an approach to improve training outcomes. *User Model User-Adap Inter.* 2015;25(1):65-98. doi:10.1007/s11257-015-9154-6
89. Sánchez-Gil JJ, Sáez-Manzano A, López-Luque R, Ochoa-Sepúlveda JJ, Cañete-Carmona E. Gamified devices for stroke rehabilitation: A systematic review.

Comput Methods Programs Biomed. 2025;258:108476.
doi:10.1016/j.cmpb.2024.108476

90. Mubin O, Alnajjar F, Al Mahmud A, Jishtu N, Alsinglawi B. Exploring serious games for stroke rehabilitation: a scoping review. *Disability and Rehabilitation: Assistive Technology.* 2022;17(2):159-165. doi:10.1080/17483107.2020.1768309
91. Cameirão MS, Badia SB i., Oller ED, Verschure PF. Neurorehabilitation using the virtual reality based Rehabilitation Gaming System: methodology, design, psychometrics, usability and validation. *Journal of NeuroEngineering and Rehabilitation.* 2010;7(1):48. doi:10.1186/1743-0003-7-48
92. Doumas I, Lejeune T, Edwards M, et al. Clinical validation of an individualized auto-adaptative serious game for combined cognitive and upper limb motor robotic rehabilitation after stroke. *J Neuroeng Rehabil.* 2025;22(1):10. doi:10.1186/s12984-025-01551-w
93. Chen R, Lv J, Qiang L, Liu X. A method for dynamically adjusting the difficulty of rehabilitation training tasks driven by attention level. *J Neural Eng.* Published online December 18, 2024. doi:10.1088/1741-2552/ada0e9
94. Sorrentino G, Edwards MG, Baldini N, Mustile M, Lejeune T, Everard G. REAsmash-ET: a methodological framework for combined cognitive and motor assessment through eye-tracking and kinematic metrics in immersive VR search-and-reach task. *J Neuroeng Rehabil.* 2025;23(1):25. doi:10.1186/s12984-025-01844-0
95. Sorrentino G, Everard G, Vanhoof F, Lejeune T, Edwards MG. A non-immersive virtual reality serious game to assess distractor inhibition and spatial attention in post-stroke individuals. *Smart Health.* 2025;37:100595. doi:10.1016/j.smhl.2025.100595
96. Sorrentino G, Ajana K, Everard G, Vanhoof F, Lejeune T, Edwards MG. The REAsmash serious game for the post-stroke diagnosis of distractor inhibition: contrast between immersive and non-immersive virtual reality test versions.

References

- Eur J Phys Rehabil Med.* 2025;61(2):197-208. doi:10.23736/S1973-9087.25.08680-0
97. Ajana K, Everard G, Sorrentino G, Lejeune T, Edwards M. *Cognitive Inhibition Difficulties in Individuals with Hemiparesis: Evidence from an Immersive Virtual Reality Target-Distractor Saliency Contrast Visual Search Serious Game.* 2023. doi:10.21203/rs.3.rs-3111608/v1
 98. Ajana K, Everard G, Lejeune T, Edwards MG. A feature and conjunction visual search immersive virtual reality serious game for measuring spatial and distractor inhibition attention using response time and action kinematics. *J Clin Exp Neuropsychol.* 2023;45(3):292-303. doi:10.1080/13803395.2023.2218571
 99. Everard G, Vermette M, Dumas-Longpré E, et al. Self-adaptive over progressive non-adaptive immersive virtual reality serious game to promote motor learning in older adults - A double blind randomized controlled trial. *Neuroscience.* 2025;571:7-18. doi:10.1016/j.neuroscience.2025.02.053
 100. Dehem S, Montedoro V, Brouwers I, et al. Validation of a robot serious game assessment protocol for upper limb motor impairment in children with cerebral palsy. *NeuroRehabilitation.* 2019;45(2):137-149. doi:10.3233/NRE-192745
 101. Duncan PW, Bushnell C, Sissine M, et al. Comprehensive Stroke Care and Outcomes: Time for a Paradigm Shift. *Stroke.* 2021;52(1):385-393. doi:10.1161/STROKEAHA.120.029678
 102. Lawrence ES, Coshall C, Dundas R, et al. Estimates of the prevalence of acute stroke impairments and disability in a multiethnic population. *Stroke.* 2001;32(6):1279-1284. doi:10.1161/01.str.32.6.1279
 103. Bogousslavsky J, Van Melle G, Regli F. The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke. *Stroke.* 1988;19(9):1083-1092. doi:10.1161/01.str.19.9.1083

104. Dutta D, Aruchamy S, Sen S, Mandal S. Prevalence of post-stroke upper extremity paresis in developing countries and significance of m-Health for rehabilitation after stroke - A review. *Smart Health*. 2022;23. doi:10.1016/j.smhl.2022.100264
105. Aben L, Heijenbrok-Kal MH, van Loon EMP, et al. Training memory self-efficacy in the chronic stage after stroke: a randomized controlled trial. *Neurorehabil Neural Repair*. 2013;27(2):110-117. doi:10.1177/1545968312455222
106. Hurford R, Charidimou A, Fox Z, Cipolotti L, Werring DJ. Domain-specific trends in cognitive impairment after acute ischaemic stroke. *J Neurol*. 2013;260(1):237-241. doi:10.1007/s00415-012-6625-0
107. Bowen A, Hazelton C, Pollock A, Lincoln NB. Cognitive rehabilitation for spatial neglect following stroke. *Cochrane Database Syst Rev*. 2013;(7):CD003586. doi:10.1002/14651858.CD003586.pub3
108. Stamenova V, Roy EA, Black SE. Associations and dissociations of transitive and intransitive gestures in left and right hemisphere stroke patients. *Brain Cogn*. 2010;72(3):483-490. doi:10.1016/j.bandc.2010.01.004
109. Bour A, Rasquin S, Limburg M, Verhey F. Depressive symptoms and executive functioning in stroke patients: a follow-up study. *Int J Geriatr Psychiatry*. 2011;26(7):679-686. doi:10.1002/gps.2581
110. Laakso HM, Hietanen M, Melkas S, et al. Executive function subdomains are associated with post-stroke functional outcome and permanent institutionalization. *Eur J Neurol*. 2019;26(3):546-552. doi:10.1111/ene.13854
111. Tennant LK, Murray NP, Tennant LM. Effects of strategy use on acquisition of a motor task during various stages of learning. *Percept Mot Skills*. 2004;98(3 Pt 2):1337-1344. doi:10.2466/pms.98.3c.1337-1344
112. Hochstenbach J, Mulder T. Neuropsychology and the relearning of motor skills following stroke. *Int J Rehabil Res*. 1999;22(1):11-19. doi:10.1097/00004356-199903000-00002

References

113. Barrett AM, Muzaffar T. Spatial cognitive rehabilitation and motor recovery after stroke. *Current Opinion in Neurology*. 2014;27(6):653. doi:10.1097/WCO.0000000000000148
114. McEwen SE, Huijbregts MPJ, Ryan JD, Polatajko HJ. Cognitive strategy use to enhance motor skill acquisition post-stroke: a critical review. *Brain Inj*. 2009;23(4):263-277. doi:10.1080/02699050902788493
115. D'Imperio D, Romeo Z, Maistrello L, et al. Sensorimotor, Attentional, and Neuroanatomical Predictors of Upper Limb Motor Deficits and Rehabilitation Outcome after Stroke. *Neural Plast*. 2021;2021:8845685. doi:10.1155/2021/8845685
116. Kim H, Kim HK, Kim N, Nam CS. Dual Task Effects on Speed and Accuracy During Cognitive and Upper Limb Motor Tasks in Adults With Stroke Hemiparesis. *Front Hum Neurosci*. 2021;15:671541. doi:10.3389/fnhum.2021.671541
117. Nijboer TCW, Kollen BJ, Kwakkel G. The impact of recovery of visuo-spatial neglect on motor recovery of the upper paretic limb after stroke. *PLoS One*. 2014;9(6):e100584. doi:10.1371/journal.pone.0100584
118. Mullick AA, Subramanian SK, Levin MF. Emerging evidence of the association between cognitive deficits and arm motor recovery after stroke: A meta-analysis. *Restor Neurol Neurosci*. 2015;33(3):389-403. doi:10.3233/RNN-150510
119. Lowrey CR, Dukelow SP, Bagg SD, Ritsma B, Scott SH. Impairments in Cognitive Control Using a Reverse Visually Guided Reaching Task Following Stroke. *Neurorehabil Neural Repair*. 2022;36(7):449-460. doi:10.1177/15459683221100510
120. Shimada H, Makizako H, Doi T, et al. Effects of Combined Physical and Cognitive Exercises on Cognition and Mobility in Patients With Mild Cognitive Impairment: A Randomized Clinical Trial. *J Am Med Dir Assoc*. 2018;19(7):584-591. doi:10.1016/j.jamda.2017.09.019

121. Fang Y, Yue GH, Hrovat K, Sahgal V, Daly JJ. Abnormal cognitive planning and movement smoothness control for a complex shoulder/elbow motor task in stroke survivors. *Journal of the Neurological Sciences*. 2007;256(1):21-29. doi:10.1016/j.jns.2007.01.078
122. Simon JR. The Effects of an Irrelevant Directional CUE on Human Information Processing. In: Proctor RW, Reeve TG, eds. *Advances in Psychology*. Vol 65. Stimulus-Response Compatibility. North-Holland; 1990:31-86. doi:10.1016/S0166-4115(08)61218-2
123. Cespón J, Hommel B, Korsch M, Galashan D. The neurocognitive underpinnings of the Simon effect: An integrative review of current research. *Cogn Affect Behav Neurosci*. 2020;20(6):1133-1172. doi:10.3758/s13415-020-00836-y
124. Ajana K, Everard G, Lejeune T, Edwards MG. A feature and conjunction visual search immersive virtual reality serious game for measuring spatial and distractor inhibition attention using response time and action kinematics. *J Clin Exp Neuropsychol*. 2023;45(3):292-303. doi:10.1080/13803395.2023.2218571
125. Treisman AM, Gelade G. A feature-integration theory of attention. *Cognitive Psychology*. 1980;12(1):97-136. doi:10.1016/0010-0285(80)90005-5
126. Plechatá A, Sahula V, Fayette D, Fajnerová I. Age-Related Differences With Immersive and Non-immersive Virtual Reality in Memory Assessment. *Front Psychol*. 2019;10:1330. doi:10.3389/fpsyg.2019.01330
127. Arlati S, Di Santo SG, Franchini F, et al. Acceptance and Usability of Immersive Virtual Reality in Older Adults with Objective and Subjective Cognitive Decline. *J Alzheimers Dis*. 2021;80(3):1025-1038. doi:10.3233/JAD-201431
128. Rafsten L, Danielsson A, Sunnerhagen KS. Anxiety after stroke: A systematic review and meta-analysis. *J Rehabil Med*. 2018;50(9):769-778. doi:10.2340/16501977-2384

References

129. Rmadi H, Maillot P, Artico R, et al. Tolerance of immersive head-mounted virtual reality among older nursing home residents. *Front Public Health*. 2023;11:1163484. doi:10.3389/fpubh.2023.1163484
130. Bickerton WL, Samson D, Williamson J, Humphreys GW. Separating forms of neglect using the Apples Test: validation and functional prediction in chronic and acute stroke. *Neuropsychology*. 2011;25(5):567-580. doi:10.1037/a0023501
131. ZIMMERMANN P, FIMM B. A test battery for attentional performance. In: *Applied Neuropsychology of Attention*. Psychology Press; 2002.
132. Ajana K, Everard G, Sorrentino G, Lejeune T, Edwards MG. *Cognitive Inhibition Difficulties in Individuals with Hemiparesis: Evidence from an Immersive Virtual Reality Target-Distractor Salience Contrast Visual Search Serious Game*. In Review; 2023. doi:10.21203/rs.3.rs-3111608/v1
133. Bohannon RW. Measurement of trunk muscle strength after stroke: An integrative review. *Top Stroke Rehabil*. 2022;29(3):173-180. doi:10.1080/10749357.2021.1904583
134. Massie CL, Malcolm MP, Greene DP, Browning RC. Kinematic motion analysis and muscle activation patterns of continuous reaching in survivors of stroke. *J Mot Behav*. 2012;44(3):213-222. doi:10.1080/00222895.2012.681321
135. Verheyden G, Vereeck L, Truijen S, et al. Trunk performance after stroke and the relationship with balance, gait and functional ability. *Clin Rehabil*. 2006;20(5):451-458. doi:10.1191/0269215505cr955oa
136. Schaefer SY, Haaland KY, Sainburg RL. Ipsilesional motor deficits following stroke reflect hemispheric specializations for movement control. *Brain*. 2007;130(Pt 8):2146-2158. doi:10.1093/brain/awm145
137. Semrau JA, Herter TM, Kenzie JM, Findlater SE, Scott SH, Dukelow SP. Robotic Characterization of Ipsilesional Motor Function in Subacute Stroke.

Neurorehabil Neural Repair. 2017;31(6):571-582.
doi:10.1177/1545968317704903

138. Sommer B, Haas M, Karrer S, et al. The Effect on Muscle Activity of Reaching Beyond Arm's Length on a Mobile Seat: A Pilot Study for Trunk Control Training for People After Stroke. *Archives of Rehabilitation Research and Clinical Translation.* 2023;5(4):100289. doi:10.1016/j.arrct.2023.100289
139. Verheyden G, Nieuwboer A, Mertin J, Preger R, Kiekens C, De Weerd W. The Trunk Impairment Scale: a new tool to measure motor impairment of the trunk after stroke. *Clin Rehabil.* 2004;18(3):326-334. doi:10.1191/0269215504cr733oa
140. Sorrentino G, Sale P, Solaro C, Rabini A, Cerri CG, Ferriero G. Clinical measurement tools to assess trunk performance after stroke: a systematic review. *Eur J Phys Rehabil Med.* 2018;54(5):772-784. doi:10.23736/S1973-9087.18.05178-X
141. Douiri A, Rudd AG, Wolfe CDA. Prevalence of poststroke cognitive impairment: South London Stroke Register 1995-2010. *Stroke.* 2013;44(1):138-145. doi:10.1161/STROKEAHA.112.670844
142. Maggio MG, Latella D, Maresca G, et al. Virtual Reality and Cognitive Rehabilitation in People With Stroke: An Overview. *J Neurosci Nurs.* 2019;51(2):101-105. doi:10.1097/JNN.0000000000000423
143. Charsky D. From edutainment to serious games: A change in the use of game characteristics. *Games and Culture: A Journal of Interactive Media.* 2010;5(2):177-198. doi:10.1177/1555412009354727
144. Bergeron BP. Developing serious games /. c2006.
145. van der Kuil MNA, Visser-Meily JMA, Evers AWM, van der Ham IJM. A Usability Study of a Serious Game in Cognitive Rehabilitation: A Compensatory Navigation Training in Acquired Brain Injury Patients. *Front Psychol.* 2018;9:846. doi:10.3389/fpsyg.2018.00846

References

146. Oliveira RS de, Trezza BM, Busse AL, Jacob-Filho W. Learning effect of computerized cognitive tests in older adults. *Einstein (Sao Paulo)*. 2014;12(2):149-153. doi:10.1590/s1679-45082014ao2954
147. Srivastava P, Rimzhim A, Vijay P, Singh S, Chandra S. Desktop VR Is Better Than Non-ambulatory HMD VR for Spatial Learning. *Front Robot AI*. 2019;6:50. doi:10.3389/frobt.2019.00050
148. Høeg ER, Povlsen TM, Bruun-Pedersen JR, et al. System Immersion in Virtual Reality-Based Rehabilitation of Motor Function in Older Adults: A Systematic Review and Meta-Analysis. *Front Virtual Real*. 2021;2. doi:10.3389/frvir.2021.647993
149. Mugambi ML, Peter T, Martins SF, Giachetti C. How to implement new diagnostic products in low-resource settings: an end-to-end framework. *BMJ Global Health*. 2018;3(6):e000914. doi:10.1136/bmjgh-2018-000914
150. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344-349. doi:10.1016/j.jclinepi.2007.11.008
151. Makransky G, Terkildsen TS, Mayer RE. Adding immersive virtual reality to a science lab simulation causes more presence but less learning. *Learning and Instruction*. 2019;60:225-236. doi:10.1016/j.learninstruc.2017.12.007
152. Makransky G, Petersen GB. The Cognitive Affective Model of Immersive Learning (CAMIL): a Theoretical Research-Based Model of Learning in Immersive Virtual Reality. *Educ Psychol Rev*. 2021;33(3):937-958. doi:10.1007/s10648-020-09586-2
153. Chandler P, Sweller J. Cognitive Load Theory and the Format of Instruction. *Cognition and Instruction*. 1991;8(4):293-332. doi:10.1207/s1532690xci0804_2
154. Jeffares I, Merriman NA, Doyle F, Horgan F, Hickey A. Designing stroke services for the delivery of cognitive rehabilitation: A qualitative study with

- stroke rehabilitation professionals. *Neuropsychol Rehabil*. 2023;33(1):24-47. doi:10.1080/09602011.2021.1977155
155. Nys GMS, Van Zandvoort MJE, De Kort PLM, et al. Domain-specific cognitive recovery after first-ever stroke: a follow-up study of 111 cases. *J Int Neuropsychol Soc*. 2005;11(7):795-806. doi:10.1017/s1355617705050952
 156. Knobel SEJ, Kaufmann BC, Gerber SM, et al. Immersive 3D Virtual Reality Cancellation Task for Visual Neglect Assessment: A Pilot Study. *Front Hum Neurosci*. 2020;14:180. doi:10.3389/fnhum.2020.00180
 157. Lumsden J, Edwards EA, Lawrence NS, Coyle D, Munafò MR. Gamification of Cognitive Assessment and Cognitive Training: A Systematic Review of Applications and Efficacy. *JMIR Serious Games*. 2016;4(2):e11. doi:10.2196/games.5888
 158. Wade DT. Measurement in neurological rehabilitation. *Curr Opin Neurol Neurosurg*. 1992;5(5):682-686.
 159. Hatem SM, Saussez G, Della Faille M, et al. Rehabilitation of Motor Function after Stroke: A Multiple Systematic Review Focused on Techniques to Stimulate Upper Extremity Recovery. *Front Hum Neurosci*. 2016;10:442. doi:10.3389/fnhum.2016.00442
 160. Stinear CM, Byblow WD, Ward SH. An update on predicting motor recovery after stroke. *Ann Phys Rehabil Med*. 2014;57(8):489-498. doi:10.1016/j.rehab.2014.08.006
 161. Michaelsen SM, Dannenbaum R, Levin MF. Task-specific training with trunk restraint on arm recovery in stroke: randomized control trial. *Stroke*. 2006;37(1):186-192. doi:10.1161/01.STR.0000196940.20446.c9
 162. Alsubiheen AM, Choi W, Yu W, Lee H. The Effect of Task-Oriented Activities Training on Upper-Limb Function, Daily Activities, and Quality of Life in Chronic Stroke Patients: A Randomized Controlled Trial. *Int J Environ Res Public Health*. 2022;19(21):14125. doi:10.3390/ijerph192114125

References

163. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. *Scand J Rehabil Med.* 1975;7(1):13-31.
164. Mathiowetz V, Volland G, Kashman N, Weber K. Adult norms for the Box and Block Test of manual dexterity. *Am J Occup Ther.* 1985;39(6):386-391. doi:10.5014/ajot.39.6.386
165. Alt Murphy M, Resteghini C, Feys P, Lamers I. An overview of systematic reviews on upper extremity outcome measures after stroke. *BMC Neurol.* 2015;15:29. doi:10.1186/s12883-015-0292-6
166. Leonardi M, Lee H, Kostanjsek N, et al. 20 Years of ICF-International Classification of Functioning, Disability and Health: Uses and Applications around the World. *Int J Environ Res Public Health.* 2022;19(18):11321. doi:10.3390/ijerph191811321
167. Platz T, Pinkowski C, van Wijck F, Kim IH, di Bella P, Johnson G. Reliability and validity of arm function assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm Test and Box and Block Test: a multicentre study. *Clin Rehabil.* 2005;19(4):404-411. doi:10.1191/0269215505cr832oa
168. Gladstone DJ, Danells CJ, Black SE. The fugl-meyer assessment of motor recovery after stroke: a critical review of its measurement properties. *Neurorehabil Neural Repair.* 2002;16(3):232-240. doi:10.1177/154596802401105171
169. See J, Dodakian L, Chou C, et al. A Standardized Approach to the Fugl-Meyer Assessment and Its Implications for Clinical Trials. *Neurorehabil Neural Repair.* 2013;27(8):732-741. doi:10.1177/1545968313491000
170. Thrane G, Sunnerhagen KS, Persson HC, Opheim A, Alt Murphy M. Kinematic upper extremity performance in people with near or fully recovered sensorimotor function after stroke. *Physiother Theory Pract.* 2019;35(9):822-832. doi:10.1080/09593985.2018.1458929

171. Santisteban L, Térémetz M, Bleton JP, Baron JC, Maier MA, Lindberg PG. Upper Limb Outcome Measures Used in Stroke Rehabilitation Studies: A Systematic Literature Review. *PLoS One*. 2016;11(5):e0154792. doi:10.1371/journal.pone.0154792
172. Cramer SC, Nelles G, Schaechter JD, Kaplan JD, Finklestein SP. Computerized measurement of motor performance after stroke. *Stroke*. 1997;28(11):2162-2168. doi:10.1161/01.str.28.11.2162
173. Nordin N, Xie SQ, Wünsche B. Assessment of movement quality in robot-assisted upper limb rehabilitation after stroke: a review. *Journal of NeuroEngineering and Rehabilitation*. 2014;11(1):137. doi:10.1186/1743-0003-11-137
174. Demers M, Levin MF. Do Activity Level Outcome Measures Commonly Used in Neurological Practice Assess Upper-Limb Movement Quality? *Neurorehabil Neural Repair*. 2017;31(7):623-637. doi:10.1177/1545968317714576
175. Schwarz A, Averta G, Veerbeek JM, et al. A functional analysis-based approach to quantify upper limb impairment level in chronic stroke patients: a pilot study. In: *2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*. 2019:4198-4204. doi:10.1109/EMBC.2019.8857732
176. Maura RM, Rueda Parra S, Stevens RE, Weeks DL, Wolbrecht ET, Perry JC. Literature review of stroke assessment for upper-extremity physical function via EEG, EMG, kinematic, and kinetic measurements and their reliability. *J Neuroeng Rehabil*. 2023;20(1):21. doi:10.1186/s12984-023-01142-7
177. Lorenz EA, Su X, Skjæret-Maroni N. A review of combined functional neuroimaging and motion capture for motor rehabilitation. *J Neuroeng Rehabil*. 2024;21:3. doi:10.1186/s12984-023-01294-6
178. Schwarz A, Kanzler CM, Lambercy O, Luft AR, Veerbeek JM. Systematic Review on Kinematic Assessments of Upper Limb Movements After Stroke. *Stroke*. 2019;50(3):718-727. doi:10.1161/STROKEAHA.118.023531

References

179. Chen C, Leys D, Esquenazi A. The interaction between neuropsychological and motor deficits in patients after stroke. *Neurology*. 2013;80(3 Suppl 2):S27-34. doi:10.1212/WNL.0b013e3182762569
180. Bártlová S, Šedová L, Havierníková L, Hudáčková A, Dolák F, Sadílek P. Quality of Life of Post-stroke Patients. *Zdr Varst*. 2022;61(2):101-108. doi:10.2478/sjph-2022-0014
181. Wall KJ, Isaacs ML, Copland DA, Cumming TB. Assessing cognition after stroke. Who misses out? A systematic review. *Int J Stroke*. 2015;10(5):665-671. doi:10.1111/ijss.12506
182. Rajda CM, Desabrais K, Levin MF. Relationships Between Cognitive Impairments and Motor Learning After Stroke: A Scoping Review. *Neurorehabil Neural Repair*. Published online November 28, 2024;15459683241300458. doi:10.1177/15459683241300458
183. Buele J, Palacios-Navarro G. Cognitive-motor interventions based on virtual reality and instrumental activities of daily living (iADL): an overview. *Front Aging Neurosci*. 2023;15:1191729. doi:10.3389/fnagi.2023.1191729
184. Wilf M, Korakin A, Bahat Y, et al. Using virtual reality-based neurocognitive testing and eye tracking to study naturalistic cognitive-motor performance. *Neuropsychologia*. 2024;194:108744. doi:10.1016/j.neuropsychologia.2023.108744
185. Oosterwijk AM, Nieuwenhuis MK, van der Schans CP, Mouton LJ. Shoulder and elbow range of motion for the performance of activities of daily living: A systematic review. *Physiother Theory Pract*. 2018;34(7):505-528. doi:10.1080/09593985.2017.1422206
186. Lamb M, Brundin M, Perez Luque E, Billing E. Eye-Tracking Beyond Peripersonal Space in Virtual Reality: Validation and Best Practices. *Front Virtual Real*. 2022;3. doi:10.3389/frvir.2022.864653
187. Faria AL, Andrade A, Soares L, i Badia SB. Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: a

- randomized controlled trial with stroke patients. *J Neuroeng Rehabil.* 2016;13:96. doi:10.1186/s12984-016-0204-z
188. Aderinto N, Olatunji G, Abdulbasit MO, Edun M, Aboderin G, Egbunu E. Exploring the efficacy of virtual reality-based rehabilitation in stroke: a narrative review of current evidence. *Ann Med.* 2023;55(2):2285907. doi:10.1080/07853890.2023.2285907
 189. Spitzley KA, Karduna AR. Feasibility of using a fully immersive virtual reality system for kinematic data collection. *J Biomech.* 2019;87:172-176. doi:10.1016/j.jbiomech.2019.02.015
 190. Tieri G, Morone G, Paolucci S, Iosa M. Virtual reality in cognitive and motor rehabilitation: facts, fiction and fallacies. *Expert Rev Med Devices.* 2018;15(2):107-117. doi:10.1080/17434440.2018.1425613
 191. Cucinella SL, de Winter JCF, Grauwmeijer E, Evers M, Marchal-Crespo L. Towards personalized immersive virtual reality neurorehabilitation: a human-centered design. *J Neuroeng Rehabil.* 2025;22:7. doi:10.1186/s12984-024-01489-5
 192. Aguilera-Rubio Á, Alguacil-Diego IM, Mallo-López A, Cuesta-Gómez A. Use of the Leap Motion Controller® System in the Rehabilitation of the Upper Limb in Stroke. A Systematic Review. *J Stroke Cerebrovasc Dis.* 2022;31(1):106174. doi:10.1016/j.jstrokecerebrovasdis.2021.106174
 193. Kwakkel G, Lannin NA, Borschmann K, et al. Standardized Measurement of Sensorimotor Recovery in Stroke Trials: Consensus-Based Core Recommendations from the Stroke Recovery and Rehabilitation Roundtable. *Neurorehabil Neural Repair.* 2017;31(9):784-792. doi:10.1177/1545968317732662
 194. Kaiser AP, Villadsen KW, Samani A, Knoche H, Evald L. Virtual Reality and Eye-Tracking Assessment, and Treatment of Unilateral Spatial Neglect: Systematic Review and Future Prospects. *Front Psychol.* 2022;13:787382. doi:10.3389/fpsyg.2022.787382

References

195. Baertsch T, Huang YY, Menozzi M. Head-mounted display versus computer monitor for visual attention screening: A comparative study. *Heliyon*. 2023;9(6):e16610. doi:10.1016/j.heliyon.2023.e16610
196. Castelhana MS. Eye movements during reading, visual search, and scene perception: An overview. In: Rayner K, ed. *Cognitive and Cultural Influences on Eye Movements*. Tianjin People's Publishing House; 2008:3-33.
197. Goettker A, Braun DI, Gegenfurtner KR. Dynamic combination of position and motion information when tracking moving targets. *J Vis*. 2019;19(7):2. doi:10.1167/19.7.2
198. Miellet S, O'Donnell PJ, Sereno SC. Parafoveal magnification: visual acuity does not modulate the perceptual span in reading. *Psychol Sci*. 2009;20(6):721-728. doi:10.1111/j.1467-9280.2009.02364.x
199. Andrychowicz-Trojanowska A. Basic terminology of eye-tracking research. *Applied Linguistics Papers*. 2018;(25/2):123-132.
200. Kovesdi C, Spielman Z, Leblanc K, Rice B. Application of eye tracking for measurement and evaluation in human factors studies in control room modernization. *Nuclear Technology*. 2018;202(2-3):220-229. doi:10.1080/00295450.2018.1455461
201. Cognolato M, Atzori M, Müller H. Head-mounted eye gaze tracking devices: An overview of modern devices and recent advances. *J Rehabil Assist Technol Eng*. 2018;5:2055668318773991. doi:10.1177/2055668318773991
202. Hougaard BI, Knoche H, Jensen J, Evald L. Spatial Neglect Midline Diagnostics From Virtual Reality and Eye Tracking in a Free-Viewing Environment. *Front Psychol*. 2021;12:742445. doi:10.3389/fpsyg.2021.742445
203. B K, K N. Assessing for Unilateral Spatial Neglect Using Eye-Tracking Glasses: A Feasibility Study. *Occupational therapy in health care*. 2016;30(4). doi:10.1080/07380577.2016.1208858

204. Machner B, Könemund I, von der Gablentz J, Bays PM, Sprenger A. The ipsilesional attention bias in right-hemisphere stroke patients as revealed by a realistic visual search task: Neuroanatomical correlates and functional relevance. *Neuropsychology*. 2018;32(7):850-865. doi:10.1037/neu0000493
205. Schwab PJ, Miller A, Raphail AM, et al. Virtual Reality Tools for Assessing Unilateral Spatial Neglect: A Novel Opportunity for Data Collection. *J Vis Exp*. 2021;(169). doi:10.3791/61951
206. Gomes Paiva AF, Sorrentino G, Bignami B, et al. Feasibility of assessing post-stroke neglect with eye-tracking glasses during a locomotion task. *Ann Phys Rehabil Med*. 2021;64(5):101436. doi:10.1016/j.rehab.2020.09.004
207. Cazzoli D, Hopfner S, Preisig B, et al. The influence of naturalistic, directionally non-specific motion on the spatial deployment of visual attention in right-hemispheric stroke. *Neuropsychologia*. 2016;92:181-189. doi:10.1016/j.neuropsychologia.2016.04.017
208. Delazer M, Sojer M, Ellmerer P, Boehme C, Benke T. Eye-Tracking Provides a Sensitive Measure of Exploration Deficits After Acute Right MCA Stroke. *Front Neurol*. 2018;9:359. doi:10.3389/fneur.2018.00359
209. Paladini RE, Wyss P, Kaufmann BC, et al. Re-fixation and perseveration patterns in neglect patients during free visual exploration. *Eur J Neurosci*. 2019;49(10):1244-1253. doi:10.1111/ejn.14309
210. Ohmatsu S, Takamura Y, Fujii S, Tanaka K, Morioka S, Kawashima N. Visual search pattern during free viewing of horizontally flipped images in patients with unilateral spatial neglect. *Cortex*. 2019;113:83-95. doi:10.1016/j.cortex.2018.11.029
211. Machner B, Dorr M, Sprenger A, et al. Impact of dynamic bottom-up features and top-down control on the visual exploration of moving real-world scenes in hemispatial neglect. *Neuropsychologia*. 2012;50(10):2415-2425. doi:10.1016/j.neuropsychologia.2012.06.012

References

212. Moon HS, Shin SW, Chung ST, Kim E. K-CBS-based unilateral spatial neglect rehabilitation training contents utilizing virtual reality. In: *2019 International Conference on Electronics, Information, and Communication (ICEIC)*. 2019:1-3. doi:10.23919/ELINFOCOM.2019.8706395
213. Primativo S, Arduino LS, De Luca M, Daini R, Martelli M. Neglect dyslexia: A matter of “good looking.” *Neuropsychologia*. 2013;51(11):2109-2119. doi:10.1016/j.neuropsychologia.2013.07.002
214. Upshaw JN, Leitner DW, Rutherford BJ, Miller HBD, Libben MR. Allocentric Versus Egocentric Neglect in Stroke Patients: A Pilot Study Investigating the Assessment of Neglect Subtypes and Their Impacts on Functional Outcome Using Eye Tracking. *J Int Neuropsychol Soc*. 2019;25(05):479-489. doi:10.1017/S1355617719000110
215. Ernst D, Wolfe JM. How fixation durations are affected by search difficulty manipulations. *Visual Cognition*. 2022;30(5):339-353. doi:10.1080/13506285.2022.2063465
216. Liu Z, Yang Z, Gu Y, Liu H, Wang P. The effectiveness of eye tracking in the diagnosis of cognitive disorders: A systematic review and meta-analysis. *PLoS One*. 2021;16(7):e0254059. doi:10.1371/journal.pone.0254059
217. Gibaldi A, Vanegas M, Bex PJ, Maiello G. Evaluation of the Tobii EyeX Eye tracking controller and Matlab toolkit for research. *Behav Res Methods*. 2017;49(3):923-946. doi:10.3758/s13428-016-0762-9
218. Tahri Sqalli M, Aslonov B, Gafurov M, Mukhammadiev N, Sqalli Houssaini Y. Eye tracking technology in medical practice: a perspective on its diverse applications. *Front Med Technol*. 2023;5:1253001. doi:10.3389/fmedt.2023.1253001
219. Ajana K, Everard G, Lejeune T, Edwards MG. A feature and conjunction visual search immersive virtual reality serious game for measuring spatial and distractor inhibition attention using response time and action kinematics. *J Clin Exp Neuropsychol*. Published online June 1, 2023:1-12. doi:10.1080/13803395.2023.2218571

220. Sorrentino G, Ajana K, Everard G, Vanhoof F, Lejeune T, Edwards MG. The REAsmash serious game for the post-stroke diagnosis of distractor inhibition: contrast between immersive and non-immersive virtual reality test versions. *Eur J Phys Rehabil Med*. Published online March 6, 2025. doi:10.23736/S1973-9087.25.08680-0
221. Everard G, Declerck L, Lejeune T, et al. A Self-Adaptive Serious Game to Improve Motor Learning Among Older Adults in Immersive Virtual Reality: Short-Term Longitudinal Pre-Post Study on Retention and Transfer. *JMIR Aging*. 2025;8:e64004. doi:10.2196/64004
222. Ptak R, Golay L, Müri RM, Schnider A. Looking left with left neglect: the role of spatial attention when active vision selects local image features for fixation. *Cortex*. 2009;45(10):1156-1166. doi:10.1016/j.cortex.2008.10.001
223. Fellrath J, Ptak R. The role of visual saliency for the allocation of attention: Evidence from spatial neglect and hemianopia. *Neuropsychologia*. 2015;73:70-81.
224. Becker SI. Determinants of Dwell Time in Visual Search: Similarity or Perceptual Difficulty? *PLoS One*. 2011;6(3):e17740. doi:10.1371/journal.pone.0017740
225. Horstmann G, Becker S, Ernst D. Perceptual salience captures the eyes on a surprise trial. *Atten Percept Psychophys*. 2016;78(7):1889-1900. doi:10.3758/s13414-016-1102-y
226. Horstmann G, Becker SI, Grubert A. Dwelling on simple stimuli in visual search. *Attention, Perception, & Psychophysics*. 2020;82(2):607-625. doi:10.3758/s13414-019-01872-8
227. Reingold EM, Glaholt MG. Cognitive control of fixation duration in visual search: The role of extrafoveal processing. *Visual Cognition*. 2014;22(3-4):610-634. doi:10.1080/13506285.2014.881443
228. Hulleman J, Lund K, Skarratt PA. Medium versus difficult visual search: How a quantitative change in the functional visual field leads to a qualitative

References

- difference in performance. *Attention, Perception, & Psychophysics*. 2020;82(1):118-139. doi:10.3758/s13414-019-01787-4
229. Horstmann G, Becker S, Ernst D. Dwelling, rescanning, and skipping of distractors explain search efficiency in difficult search better than guidance by the target. *Visual Cognition*. 2017;25(1-3):291-305. doi:10.1080/13506285.2017.1347591
230. Pouke M, Tiirio A, LaValle S, Ojala T. *Effects of Visual Realism and Moving Detail on Cybersickness*. 2018:666. doi:10.1109/VR.2018.8446078
231. Ang S, Quarles J. Reduction of cybersickness in head mounted displays use: A systematic review and taxonomy of current strategies. *Front Virtual Real*. 2023;4. doi:10.3389/frvir.2023.1027552
232. Kim N, Grégoire L, Razavi M, et al. Protocol to evaluate the effectiveness of a virtual-reality-based behavioral intervention in enhancing sensory responses to real-world warning. *STAR Protoc*. 2024;5(3):103262. doi:10.1016/j.xpro.2024.103262
233. VIVE Pro Eye Specs & User Guide - Developer Resources. Accessed September 17, 2025. <https://developer.vive.com/resources/hardware-guides/vive-pro-eye-specs-user-guide/>
234. Schuetz I, Fiehler K. Eye Tracking in Virtual Reality: Vive Pro Eye Spatial Accuracy, Precision, and Calibration Reliability. *J Eye Mov Res*. 15(3):10.16910/jemr.15.3.3. doi:10.16910/jemr.15.3.3
235. Niehorster DC, Li L, Lappe M. The accuracy and precision of position and orientation tracking in the HTC vive virtual reality system for scientific research. *i-Perception*. 2017;8(3). doi:10.1177/2041669517708205
236. Sansone LG, Stanzani R, Job M, Battista S, Signori A, Testa M. Robustness and static-positional accuracy of the SteamVR 1.0 virtual reality tracking system. *Virtual Reality*. 2022;26(3):903-924. doi:10.1007/s10055-021-00584-5

237. Llanes-Jurado J, Marín-Morales J, Guixeres J, Alcañiz M. Development and Calibration of an Eye-Tracking Fixation Identification Algorithm for Immersive Virtual Reality. *Sensors (Basel)*. 2020;20(17):4956. doi:10.3390/s20174956
238. J. Llanes-Jurado, J. Marín-Morales, J. Guixeres, and M. Alcañiz. Vrcentred-i-dt-algorithm. https://github.com/ASAPLableni/VR-centred_I-DT_algorithm, 2020.
239. Roche AF, Martorell (eds) R. *Anthropometric Standardization Reference Manual*. Human Kinetics Books; 1988.
240. Blignaut P. Fixation identification: the optimum threshold for a dispersion algorithm. *Atten Percept Psychophys*. 2009;71(4):881-895. doi:10.3758/APP.71.4.881
241. Carpenter RHS. *Movements of the Eyes*. Pion; 1988.
242. Salthouse TA, Ellis CL. Determinants of eye-fixation duration. *Am J Psychol*. 1980;93(2):207-234.
243. van Renswoude DR, Raijmakers MEJ, Koornneef A, Johnson SP, Hunnius S, Visser I. Gazepath: An eye-tracking analysis tool that accounts for individual differences and data quality. *Behav Res*. 2018;50(2):834-852. doi:10.3758/s13428-017-0909-3
244. Manor BR, Gordon E. Defining the temporal threshold for ocular fixation in free-viewing visuocognitive tasks. *J Neurosci Methods*. 2003;128(1-2):85-93. doi:10.1016/s0165-0270(03)00151-1
245. Salvucci DD, Goldberg JH. Identifying fixations and saccades in eye-tracking protocols. In: *Proceedings of the 2000 Symposium on Eye Tracking Research & Applications*. ETRA '00. Association for Computing Machinery; 2000:71-78. doi:10.1145/355017.355028
246. Kaufmann BC, Knobel SEJ, Nef T, Müri RM, Cazzoli D, Nyffeler T. Visual Exploration Area in Neglect: A New Analysis Method for Video-Oculography

References

- Data Based on Foveal Vision. *Front Neurosci.* 2020;13:1412. doi:10.3389/fnins.2019.01412
247. Cazzoli D, Nyffeler T, Hess CW, Müri RM. Vertical bias in neglect: a question of time? *Neuropsychologia.* 2011;49(9):2369-2374. doi:10.1016/j.neuropsychologia.2011.04.010
248. Ptak R, Bourgeois A. Disengagement of attention with spatial neglect: A systematic review of behavioral and anatomical findings. *Neurosci Biobehav Rev.* 2024;160:105622. doi:10.1016/j.neubiorev.2024.105622
249. Lawrence RK, Edwards M, Goodhew SC. Changes in the spatial spread of attention with ageing. *Acta Psychol (Amst).* 2018;188:188-199. doi:10.1016/j.actpsy.2018.06.009
250. Balasubramanian S, Melendez-Calderon A, Roby-Brami A, Burdet E. On the analysis of movement smoothness. *J Neuroeng Rehabil.* 2015;12:112. doi:10.1186/s12984-015-0090-9
251. Mohamed Refai MI, Saes M, Scheltinga BL, et al. Smoothness metrics for reaching performance after stroke. Part 1: which one to choose? *J Neuroeng Rehabil.* 2021;18:154. doi:10.1186/s12984-021-00949-6
252. Wiegand I, van Pouderoijen M, Oosterman JM, Deckers K, Horstmann G. Contributions of distractor dwelling, skipping, and revisiting to age differences in visual search. *Sci Rep.* 2025;15(1):1801. doi:10.1038/s41598-024-83532-y
253. Rayner K. Eye movements and attention in reading, scene perception, and visual search. *Q J Exp Psychol (Hove).* 2009;62(8):1457-1506. doi:10.1080/17470210902816461
254. Hooge IT, Erkelens CJ. Control of fixation duration in a simple search task. *Percept Psychophys.* 1996;58(7):969-976. doi:10.3758/bf03206825
255. Spaccavento S, Marinelli CV, Nardulli R, et al. Attention Deficits in Stroke Patients: The Role of Lesion Characteristics, Time from Stroke, and

- Concomitant Neuropsychological Deficits. *Behav Neurol*. 2019;2019:7835710. doi:10.1155/2019/7835710
256. Coll SY, Marti E, Doganci N, Ptak R. The disengagement deficit after right-hemisphere damage: Distinct roles of lateral frontal and parietal damage. *Brain Res Bull*. 2024;214:111003. doi:10.1016/j.brainresbull.2024.111003
 257. Lugtmeijer S, Lammers NA, de Haan EHF, de Leeuw FE, Kessels RPC. Post-Stroke Working Memory Dysfunction: A Meta-Analysis and Systematic Review. *Neuropsychol Rev*. 2021;31(1):202-219. doi:10.1007/s11065-020-09462-4
 258. Collins KC, Kennedy NC, Clark A, Pomeroy VM. Kinematic Components of the Reach-to-Target Movement After Stroke for Focused Rehabilitation Interventions: Systematic Review and Meta-Analysis. *Front Neurol*. 2018;9:472. doi:10.3389/fneur.2018.00472
 259. Choi H, Park D, Rha DW, Nam HS, Jo YJ, Kim DY. Kinematic analysis of movement patterns during a reach-and-grasp task in stroke patients. *Front Neurol*. 2023;14:1225425. doi:10.3389/fneur.2023.1225425
 260. Adhanom IB, MacNeilage P, Folmer E. Eye Tracking in Virtual Reality: a Broad Review of Applications and Challenges. *Virtual Reality*. 2023;27(2):1481-1505. doi:10.1007/s10055-022-00738-z
 261. Everard G, Vermette M, Dumas-Longpré E, et al. Self-adaptive over progressive non-adaptive immersive virtual reality serious game to promote motor learning in older adults – A double blind randomized controlled trial. *Neuroscience*. 2025;571:7-18. doi:10.1016/j.neuroscience.2025.02.053
 262. Clark L, El Iskandarani M, Riggs S. Reaching interactions in virtual reality: the effect of movement direction, hand dominance, and hemispace on the kinematic properties of inward and outward reaches. *Virtual Reality*. 2024;28. doi:10.1007/s10055-023-00930-9

References

263. Tales A, Snowden RJ, Haworth J, Wilcock G. Abnormal spatial and non-spatial cueing effects in mild cognitive impairment and Alzheimer's disease. *Neurocase*. 2005;11(1):85-92. doi:10.1080/13554790490896983
264. Rinaldi L, Di Luca S, Henik A, Girelli L. Reading direction shifts visuospatial attention: an Interactive Account of attentional biases. *Acta Psychol (Amst)*. 2014;151:98-105. doi:10.1016/j.actpsy.2014.05.018
265. Fagard J, Dahmen R. The effects of reading-writing direction on the asymmetry of space perception and directional tendencies: a comparison between French and Tunisian children. *Laterality*. 2003;8(1):39-52. doi:10.1080/713754473
266. Smith AK, Szelest I, Friedrich TE, Elias LJ. Native reading direction influences lateral biases in the perception of shape from shading. *Laterality*. 2015;20(4):418-433. doi:10.1080/1357650X.2014.990975
267. Heilman KM, Watson RT, Valenstein E. Spatial neglect. In: *The Cognitive and Neural Bases of Spatial Neglect*. Oxford University Press; 2002:3-30. doi:10.1093/acprof:oso/9780198508335.003.0001
268. Yao Z, Zhang T, Chen F, et al. Cognitive Function and Upper Limb Rehabilitation Training Post-Stroke Using a Digital Occupational Training System. *J Vis Exp*. 2023;(202). doi:10.3791/65994
269. Meadmore KL, Hallowell E, Freeman C, Hughes AM. Factors affecting rehabilitation and use of upper limb after stroke: views from healthcare professionals and stroke survivors. *Top Stroke Rehabil*. 2019;26(2):94-100. doi:10.1080/10749357.2018.1544845
270. Fernandes JB, Fernandes S, Domingos J, et al. Motivational strategies used by health care professionals in stroke survivors in rehabilitation: a scoping review of experimental studies. *Front Med*. 2024;11. doi:10.3389/fmed.2024.1384414
271. Soni AK, Kumar M, Kothari S. Efficacy of home based computerized adaptive cognitive training in patients with post stroke cognitive impairment:

- a randomized controlled trial. *Sci Rep*. 2025;15(1):1072. doi:10.1038/s41598-025-85511-3
272. Yang ZQ, Du D, Wei XY, Tong RKY. Augmented reality for stroke rehabilitation during COVID-19. *Journal of NeuroEngineering and Rehabilitation*. 2022;19(1):136. doi:10.1186/s12984-022-01100-9
 273. Quan W, Liu S, Cao M, Zhao J. A Comprehensive Review of Virtual Reality Technology for Cognitive Rehabilitation in Patients with Neurological Conditions. *Applied Sciences*. 2024;14(14):14. doi:10.3390/app14146285
 274. Bevilacqua R, Maranesi E, Riccardi GR, et al. Non-Immersive Virtual Reality for Rehabilitation of the Older People: A Systematic Review into Efficacy and Effectiveness. *J Clin Med*. 2019;8(11):1882. doi:10.3390/jcm8111882
 275. Shahmoradi L, Mohammadian F, Rahmani Katigari M. A Systematic Review on Serious Games in Attention Rehabilitation and Their Effects. *Behav Neurol*. 2022;2022:2017975. doi:10.1155/2022/2017975
 276. Zhang Q, Fu Y, Lu Y, et al. Impact of Virtual Reality-Based Therapies on Cognition and Mental Health of Stroke Patients: Systematic Review and Meta-analysis. *Journal of Medical Internet Research*. 2021;23(11):e31007. doi:10.2196/31007
 277. O'Donoghue M, Leahy S, Boland P, Galvin R, McManus J, Hayes S. Rehabilitation of Cognitive Deficits Poststroke: Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Stroke*. 2022;53(5):1700-1710. doi:10.1161/STROKEAHA.121.034218
 278. Glegg SMN, Levac DE. Barriers, Facilitators and Interventions to Support Virtual Reality Implementation in Rehabilitation: A Scoping Review. *PM R*. 2018;10(11):1237-1251.e1. doi:10.1016/j.pmrj.2018.07.004
 279. Xue S, Wu M, Kolen J, Aghdaie N, Zaman K. *Dynamic Difficulty Adjustment for Maximized Engagement in Digital Games*. 2017:471. doi:10.1145/3041021.3054170

References

280. Guzmán DE, Rengifo CF, Guzmán JD, Garcia Cena CE. Virtual reality games for cognitive rehabilitation of older adults: a review of adaptive games, domains and techniques. *Virtual Reality*. 2024;28(2):92. doi:10.1007/s10055-024-00968-3
281. Mishra J, Gazzaley A. Harnessing the neuroplastic potential of the human brain & the future of cognitive rehabilitation. *Front Hum Neurosci*. 2014;8. doi:10.3389/fnhum.2014.00218
282. Khokale R, Mathew G, Ahmed S, et al. Virtual and Augmented Reality in Post-stroke Rehabilitation: A Narrative Review. *Cureus*. 2023;15. doi:10.7759/cureus.37559
283. van der Kooij K, In 't Veld L, Hennink T. Motivation as a function of success frequency. *Motiv Emot*. 2021;45(6):759-768. doi:10.1007/s11031-021-09904-3
284. Castro Lopes J, Lopes R. A Review of Dynamic Difficulty Adjustment Methods for Serious Games. In: 2023:144-159. doi:10.1007/978-3-031-23236-7_11
285. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ*. 2014;348:g1687. doi:10.1136/bmj.g1687
286. Dharmasaroja PA. Temporal Changes in Cognitive Function in Early Recovery Phase of the Stroke. *J Stroke Cerebrovasc Dis*. 2021;30(10):106027. doi:10.1016/j.jstrokecerebrovasdis.2021.106027
287. The Safe Harbor Method of De-Identification. Satori. Accessed March 25, 2026. <https://satoricyber.com/data-classification/the-safe-harbor-method-of-de-identification-2/>
288. Adam KCS, Patel T, Rangan N, Serences JT. Classic Visual Search Effects in an Additional Singleton Task: An Open Dataset. *J Cogn*. 4(1):34. doi:10.5334/joc.182

289. Ajana K, Everard G, Sorrentino G, Lejeune T, Edwards M. *Cognitive Inhibition Difficulties in Individuals with Hemiparesis: Evidence from an Immersive Virtual Reality Target-Distractor Salience Contrast Visual Search Serious Game*. 2023. doi:10.21203/rs.3.rs-3111608/v1
290. Ajana K. *Innovations in Neuropsychology Assessment Methods Using Immersive Virtual Reality*. UCLouvain; 2023. Accessed May 4, 2026. <https://hdl.handle.net/2078.5/29844>
291. Everard G. *Virtual Reality to Improve Assessment and Rehabilitation in Stroke Rehabilitation*. UCLouvain; 2022. Accessed May 4, 2026. <https://hdl.handle.net/2078.5/102016>
292. Gaspelin N, Luck SJ. The Role of Inhibition in Avoiding Distraction by Salient Stimuli. *Trends Cogn Sci*. 2018;22(1):79-92. doi:10.1016/j.tics.2017.11.001
293. Luck SJ, Gaspelin N, Folk CL, Remington RW, Theeuwes J. Progress Toward Resolving the Attentional Capture Debate. *Vis cogn*. 2021;29(1):1-21. doi:10.1080/13506285.2020.1848949
294. Vítěková L, Eichhorn C, Pirker J, Plecher DA. Dynamic Difficulty Adjustment in Serious Games: A Literature Review. *Information*. 2026;17(1):96. doi:10.3390/info17010096
295. Chan ATC, Ip RTF, Tran JYS, Chan JYC, Tsoi KKF. Computerized cognitive training for memory functions in mild cognitive impairment or dementia: a systematic review and meta-analysis. *npj Digit Med*. 2024;7(1):1. doi:10.1038/s41746-023-00987-5
296. Gillespie KM, Dymond AH, Li X, et al. A Systematic Review and Narrative Synthesis of Cognitive Training in the Treatment of Mental Illness and Substance Use Disorder. *Journal of Clinical Medicine*. 2024;13(15):4348. doi:10.3390/jcm13154348

References

297. Mele ML, Federici S. Gaze and Eye-Tracking Perspectives for Psychological Research: A Narrative Review of Advances From 2012 to 2025. *Cureus*. 2026;18:e104753. doi:10.7759/cureus.104753