Using a game-based screening for Mild Cognitive Impairment detection

Farnaz Koubasi

Ph.D. candidate in Rehabilitation Sciences

University of Alberta

Supervisor: Dr. Adriana Rios Rincon

Co-supervisor: Dr. Shaniff Esmail

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Table of Contents

1. Introduction *4*

1.1 Background 4

1.2 Significance of this study 7

1.3 Research questions 8

2.1. Cognition 9

2.1.1 Definition and different domains 9
2.1.2 Processing speed 10
2.1.3 Attention 11
2.1.4 Memory 11
2.1.5 Visuospatial skills 13
2.1.6 Executive functions 13
2.1.7 Language 14

2.2 MCI 14

2.2.1 Definition, prevalence, and its classification 14
2.2.3 Brain structural and functional changes in typical aging vs in MCI 16
2.2.4 Cognitive changes associated with typical aging VS MCI 16
2.2.5 MCI diagnosis 20
2.2.6 Advantages and disadvantages of cognitive tests 22
2.2.7 Summary and gaps 23

2.3 Digital technology for MCI screening 24

2.3.1 Digital technologies 24
2.3.2 Digital biomarkers 26
2.3.3 Serious Computer Games and their classification 27
2.3.4 The advantages and disadvantages of Serious Computer Games compared to traditional cognitive tests 28
2.3.5 Serious Computer Games as screening tools for MCI 31
2.3.6 Summary and gaps 36

3. Method *38*

3.1 Study design 38

3.2 Participants 38

3.2.1 Inclusion criteria 38
3.2.2 Exclusion criteria 39

3.3 Sample size 39

3.4 Sampling strategy 41

3.5 Settings and Materials 41

3.5.1 Settings 41

3.5.2 Materials 41

3.6 Variables 42

3.7 Recruitment 45

3.8 Data collection 46

3.9 Data analysis **48**
3.10 Ethical considerations **51**
3.11 Limitations **52**
3.12 Timeline **53**
3.13 Budget **53**
References ***54***

1. Introduction

1.1 Background

As global life expectancy continues to rise, the number of older adults also increase (1). The global population of individuals aged 65 and older is expected to surge from 761 million in 2021 to 1.6 billion by the year 2050, highlighting a significant demographic shift (2). The aging trend leads to a significant rise in the prevalence of cognitive impairments, notably Mild Cognitive Impairment (MCI) and dementia. Dementia, is a progressive syndrome that damages the brain, leading to a decline in cognitive function, behaviour, and ability to perform Activities of Daily Livings (ADL) beyond what is typically expected from normal aging (3). Dementia has significant physical, psychological, social and economic impacts on individuals living with this condition, as well as on their care givers, families and society (3). Dementia affects nearly half a million Canadians aged 65 and older (4). Given dementia's status as a significant cause of disability and dependency among older adults, and as the 7th leading cause of death globally, the World Health Organization has prioritized dementia as a public health concern (3).

MCI often represents a critical transitional stage between normal aging and dementia (5). Unlike normal aging, which involves gradual cognitive decline without significant impact on daily living activities, MCI causes notable reductions in cognitive abilities, particularly affecting instrumental Activities of Daily living (iADL) (6). Importantly, 10% to 15% of individuals with MCI annually progress to dementia (7)- significantly higher than the 1% to 2% incidence annually in the general population, and up to 18% revert to normal cognitive status (8).

Early detection MCI is consistent with the goal of high-quality health care. It facilitates timely access to information and treatments (9,10). It also allows for the modification of risk factors like smoking, physical inactivity, and social isolation, potentially delaying disease progression (11).

Additionally, it assists in identifying potential participants for research, essential for evaluating new treatments (9,12). Early detection also allows the patients to discuss their situation with clinicians and family members, insights into prognosis, care preferences, and future financial and living arrangements plans (9,10).

However, early detection of MCI is challenging. Individuals who notice cognitive difficulties or their families often seek assessment from Primary Care Physicians (PCPs) (13). Unfortunately, PCPs currently lack the technical support, time, training, and experience to efficiently detect cognitive impairments from preclinical phases to MCI and dementia (14,15). Research has shown that cognitive evaluation might also be skipped due to subtle cognitive impairment, fear of stigma, and patient resistance to testing (14). Currently, MCI diagnosis primarily relies on patients' history, neurological examinations, and to a great extent, traditional cognitive tests (13). Traditional cognitive tests are usually a part of the process of diagnosing MCI. These tests, such as the Montreal Cognitive Assessment (MoCA) (16), Mini Mental State Examination (MMSE) (17), and Saint Louis University Mental Status Examination (SLUMS) (18) can distinguish cognitive impairment from normal aging (19). They are often administered in paper-and-pencil format, which is straightforward and familiar for older adults. However, they have some limitations. Subjective scoring could introduce human errors (20). These tests often fail to represent the complexity of real-life tasks (21). Moreover, the need for trained clinicians to administer the test restricts access and make continuous monitoring both difficult and costly (22,23). Additionally, these tests might induce anxiety in older adults (24), potentially leading to test avoidance or negatively affecting their cognitive performance (25).These limitations highlight the need to investigate new, more accessible and less stressful complementary tools for MCI detection (13).

In response to these diagnostic challenges, there is a growing interest in leveraging digital technologies to enhance the accuracy, accessibility, and efficiency of MCI detection. These technologies include wearable devices, home/car embedded sensors, Artificial Intelligence (AI) algorithms, mobile apps and computerized tests, Virtual Reality (VR), and Serious Computer Games (SCG) (9,26,27). Wearable devices and embedded sensors are advantageous due to their ability to provide continuous data on cognitive and functional changes. However, utilizing complex algorithms and handling large data volumes, which are still areas under active development, will be required for analysis and interpretation of the data (9). VR offers an immersive experience that could potentially benefit cognitive assessments by simulating real-life environments and tasks. However, the requirement for users to wear cumbersome head mounted displays can lead to discomfort and cybersickness (28,29) besides the high costs and accessibility barriers associated with VR systems (30).

SCGs are fully-fledged games designed for purposes beyond entertainment (31). The integration of digital technologies with the capabilities of data tracking (9) and the growing positive attitude toward video games among older adults (32) make SCGs a promising tool for cognitive screening in older adults. Studies have shown that SCGs can effectively differentiate between healthy individuals and those with MCI (22,33–36), offering a non-invasive, accessible, and engaging method for early detection. These games can be administered cost-effectively and remotely, allowing for frequent monitoring without the need for clinical visits (22,23,37). The data collected from SCGs can be used to track cognitive changes over time, enabling timely interventions.

Computerized tests and Mobile apps also share benefits such as being time-efficient, inexpensive, and accessible. They can be administered with minimal training and are particularly suitable for remote settings. Finally, in contrast to computerized cognitive tests and some apps that often mirror traditional cognitive tests, SCGs incorporate elements of gamification that enhance engagement and participation, making them more appealing and less monotonous for users (27).

1.2 Significance of this study

Despite promising applications of SCGs, several research gaps remain. The validities of the applied SCGs are not excellent, and demographic variables, as potential factors associated with cognitive status have been often overlooked. This highlights the need for more comprehensive research to understand how these factors might influence game-based cognitive screenings. Variability in game scenarios and small sample sizes limit the generalizability of findings. Additionally, some tested games lack alignment with older adults' needs and daily tasks or require physical demands that may pose challenges (38). Many applied SCGs were initially developed for healthy users and repurposed for those with cognitive impairments, lacking components simulating daily activities and compelling narratives to motivate maximum performance (39,40). Furthermore, the MMSE has been widely used in numerous studies (39,41), but it is not a precise screening for MCI (42). Investigating the psychological impact, such as state anxiety, of game-based versus traditional screenings has never been examined. In terms of usability, only two previous studies have investigated the usability of game-based screenings for MCI detection, demonstrating good usability for games using touch screens and simulating daily routine (43,44). However, the usability of SCGs using other delivery modes, like computers and mice, has not been explored. Usability is highly dependent on the specific game and its features, necessitating further assessment of different SCGs to confirm their usability for older adults.

A promising game developed in Alberta, called the Glenrose Grocery Game (G3), has been designed for older adults' cognitive training that could address these limitations. This game, commercially available for free, mimics the grocery shopping experience in a real-life scenario, offering a potentially valuable tool for cognitive assessment. G3's design has the potential to addresses previous limitations by focusing on an iADL (grocery shopping) in a virtual environment and avoiding reliance on informants' reports, and subjective scoring. G3 has been tailored to challenge cognitive skills such as attention, memory, and executive functions, which are often impaired in MCI. Thus, G3 is expected to serve as an effective proxy for detecting MCI. G3 could also be accessible for individuals living in remote areas or without internet access. The proposed study aims to address a few of the discussed gaps by investigating the feasibility of (G3), a game-based screening designed specifically for older adults, for MCI detection.

1.3 Research questions

The present study aims to respond the following research questions (RQ).

1. Is there any difference between the game performance of older adults with typical cognition and individuals with MCI?

2. What is the concurrent validity of the game-based screening for MCI detection?

    2.1 Is there any relationship between game performance and total score of traditional cognitive tests (MoCA score and Quick MCI (Qmci)) in older adults with typical cognitive and older adults with MCI?

    2.2 Is there any relationship between the sub-MoCA scores and sub-Qmci scores and the game metrics in older adults with typical cognitive and older adults with MCI?

3.What is the diagnostic accuracy of the game-based screening assessed by sensitivity, specificity, accuracy, and the Area Under Curve (AUC) of the game-based screening for MCI detection?

4. Is game performance an associated factor with cognitive status controlled by demographic variables?

5. Is there any difference between the level of state anxiety while playing the G3 game and while administering traditional cognitive tests in older adults with typical cognition and individuals with MCI?

6. What is the usability of the G3 as a game-based screening?

2. Literature review

This chapter will address several key areas essential for understanding the use of SCGs in cognitive screening for MCI. It will begin with an overview of cognitive functions and their domains, followed by a discussion of MCI, its prevalence, and associated brain changes. The review will then examine cognitive changes with aging and MCI, traditional cognitive tests used for MCI diagnosis, and their limitations. It will explore digital technologies for MCI screening, focusing on the potential of SCGs. Finally, the chapter will highlight research gaps and propose directions future studies, emphasizing the investigation of the G3, a SCG designed for older adults, for MCI detection.

2.1. Cognition

2.1.1 Definition and different domains

Cognition is defined as various mental activities involved in acquiring, storing, manipulating, and retrieving information (45). Cognitive functions allow us to learn from past experiences, plan for the future, and handle complex social interactions. Without robust cognitive capabilities, our capacity to interact with others, accomplish tasks, and meet personal and professional objectives would be greatly affected (45). Cognitive performance is often described through various functional domains that form a hierarchy. At the lower levels are fundamental sensory and perceptual processes, while higher levels involve aspects of executive functions. These domains are interrelated, with executive functions regulating the use of more basic processes (46). This proposal will discuss six primary cognitive domains including processing speed, attention, memory, visuospatial skills, executive function, and language.

2.1.2 Processing speed

Processing speed is a foundational aspect of cognitive performance, encompassing the rate at which a person can execute cognitive tasks and motor responses. It stands out as a primary predictor of overall cognitive performance (47). This broader concept of processing speed is linked to specific metrics as follows: 1. Decision speed refers to how quickly an individual responds to complex cognitive tests, reflecting not just speed but also cognitive ability; 2. Perceptual speed refers to response times to simpler, often paper-and-pencil tests; 3. Psychomotor speed involves tasks like repetitive actions, such as finger tapping or drawing lines; 4. Reaction time is defined by how quickly one responds to visual stimuli; 5. Psychophysical speed refers to the accuracy in making decisions based on brief visual or auditory inputs, like quickly identifying an object; 6. Psychophysiological speed looks at internal response times, such as the latency in specific brain response components. These components of processing speed not only reflect the ability to perform tasks swiftly but also the accuracy and efficiency with which the brain and body respond to different types of stimuli, thus demonstrating the holistic impact of processing speed on cognitive functions (47).

2.1.3 Attention

Attention encompasses selective attention, divided attention, and sustained attention. Selective attention refers to attending to important information while there are other distractors available. Divided attention facilitates performing dual tasks, when two simultaneous pieces of information are being processed. In this situation, an individual could either prioritize paying more attention to one of the tasks or optimize their attention on both. Sustained attention refers to the capacity to maintain attention over an extended period (46). Attention is crucial for learning as it facilitates selective awareness and narrows focus on specific aspects of the sensory environment, such as having a conversation in a noisy room while filtering out distractors. Attention also helps us process and respond more efficiently to critical information, thereby optimizing our cognitive functions for both survival and everyday activities (45).

2.1.4 Memory

Memory is not solely a revival of past experiences; it is an active process of the registration of all combined mental experiences and encoding them into different systems (48). Memory can be categorized into Sensory Memory, Short-Term Memory (STM), Working Memory (WM), and Long-Term Memory (LTM) (49). Sensory memory serves as an automatic storage of sensory information memory. It is an immediate form of memory that captures the sights, sounds, textures, smells, and tastes we experience, providing us with a real-time view of the world (49). STM can temporarily hold limited information in a very accessible way, for example, remembering the alphabets that were shown for a few milliseconds (50). WM is defined as the processes the brain uses to understand, modify, interpret, and store information in STM. WM is closely related to STM and executive functions, consisting of several interconnected components for visuospatial and verbal stimuli. It temporarily holds and manipulates information, unlike

STM which only retains information. WM involves the use of memory to plan and execute actions (51,52), for example remembering the numbers to add them up. LTM refers to the unlimited storage of unlimited information. It includes declarative (explicit), non-declarative (implicit), and emotional memory (a combination of implicit and explicit). Explicit memory encompasses episodic and semantic memory. Episodic memory, a declarative memory, involves recollecting personal experiences with their temporal and spatial details, for example remembering the memory of a birthday party (45,53,54). Semantic memory is another type of declarative memory which handles general knowledge and learning during life, for example learning science at school. Implicit memory includes procedural memory that involves both sensorimotor and cognitive functions, such as learning to ride a bike. It works unconsciously, with automatic retrieval of information (45,53,54). Finally, emotional memory, another type of LTM, is the ability to remember experiences that are associated with strong emotions, such as remembering an event where we were so angry. Emotional memory is often more vivid and lasting compared to episodic memory, involving both implicit and explicit memory systems. Emotional memories can also influence behavior and decision-making, often guiding how individuals react to similar situations in the future (45). Memory as a whole plays an indispensable role in retaining and recalling past life experiences, serving as the foundation for learning, decision-making, and problem-solving. Memory also involves in language use, enabling us to remember vocabulary and apply language rules. Furthermore, memory provides a sense of continuity, helping us remember personal histories, past feelings, and cultural knowledge, which shapes our identity and influences how we view the world and interact with others (45).

2.1.5 Visuospatial skills

Visuospatial skills contribute to holding and recalling basic visuospatial information, such as the color and distance of objects. Additionally, mental imagery, another visuospatial skill, involves creating a vivid and realistic image of objects and scenes that are not present. At a more advanced level, these skills play a role in navigation and self-orientation (55). Visuospatial abilities contribute to daily activities including tasks like wayfinding, orientation, using maps, detecting the locations of objects, and reaching them. This skill is an indispensable part of carrying out independent movements within the environment. Additionally, there is a link between episodic memory and spatial abilities in the creation of memories associated with particular spatial contexts (55).

2.1.6 Executive functions

Executive functions, also known as executive control, are top-down mental processes vital for maintaining focus when instinctive responses are insufficient. Executive functions, including inhibitory control and mental flexibility, are essential for complex tasks such as reasoning, planning, and problem-solving, all of which require considerable effort (56). Inhibitory control involves managing attention, behavior, thoughts, and emotions, contributing to intentional actions beyond automatic responses. This capacity contributes to intentional reactions beyond conditional responses, habits, and impulsive behaviors. Mental flexibility contributes to creativity by enabling one to change perspectives, adapt to new situations, and seize opportunities. Both inhibitory control and mental flexibility are closely linked to each other as well as to WM. This coordination enables independent, purposeful behavior, enhancing mental and physical health, educational success, job success, marital harmony, and overall quality of life (56).

2.1.7 Language

Language abilities include both understanding and expressing language, accessing memory for meaning, identifying objects by name, and reacting to spoken commands with specific actions (46). Language encompasses four main skills, including: 1. Categorizing: this skill involves grouping similar objects, ideas, or information together, which helps in organizing knowledge and simplifying communication by managing complex sets of information into simpler, more understandable units; 2. Labelling categories: After categorizing items, assigning labels to these categories facilitates communication. This process allows for efficient and effective exchange of ideas by using specific words or phrases to represent entire groups of related items; 3. Sequencing behavior: This skill is about arranging language elements in a logical and meaningful order. It is essential for clarity in communication, enabling the construction of coherent messages, stories, instructions, and arguments; 4. Mimicry: In language, mimicry refers to the imitation of sounds, words, phrases, and language patterns, which is crucial for learning and adapting language. It helps in acquiring linguistic norms and enhances social interaction (45).

2.2 MCI

2.2.1 Definition, prevalence, and its classification

MCI is characterized as a cognitive impairment that exceeds normal age-related decline but is not severe enough to substantially affect daily functioning (57–59). MCI often emerges with memory and learning deficiency (60), and it usually progresses to other cognitive impairments (5). The first clinical criteria for MCI were suggested by the researchers from the Mayo Clinic in the late 1990s. These criteria originally pinpointed memory impairment while maintaining other cognitive functions. The criteria encompass memory issues, verified by an informant, intact general cognition; unimpaired activities of daily living; and the absence of dementia (61).

Subsequent studies have broadened the symptoms of MCI to include other cognitive domains, leading to the development of the Petersen Criteria (62). Petersen criteria are characterized by a cognitive complaint, preferably confirmed by an informant, intact global cognition, unimpaired ADL, and absence of dementia, without significant disruption of iADL (62). However, subtle challenges in iADL might be evident (63). The Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-V) also characterizes MCI as a “mild neurocognitive disorder.” It requires both subjective and objective cognitive decline compared to the prior level of cognitive abilities but is not defined as dementia or other psychological disorders (64).

The prevalence of MCI varies widely, ranging from 0.5% to 41.8% (65), with an overall prevalence of 19.7% in the world (66). Risk increases with age, and men appear to be at higher risk than women (67). Additionally, lower educational level, vascular risk factors (e.g., diabetes and hypertension), Apolipoprotein E (APOE) e4 genotype, vitamin D deficiency, sleep-disordered breathing, and prior critical illness (e.g., sepsis) are other risk factors for MCI (68,69). Classification of MCI is challenging due to its heterogeneous nature. However, it could be classified based on either etiology or the existence of memory impairment (61). Based on etiology MCI is classified into 1. MCI associated with Alzheimer's Disease (AD) which is associated mostly with memory decline. However, it might affect other cognitive domains as well (70); 2. Vascular MCI (VMCI) is related to issues with blood vessels in the brain, affecting multiple cognitive functions (71); 3. MCI caused by Parkinson's Disease (PD-MCI) represents a transitional state between normal cognition and dementia in Parkinson's disease, affecting either memory or other cognitive domains or even both memory and other cognitive domains (72). MCI is also classified based on the presence of memory impairment. It is divided into amnestic (aMCI), involving memory decline with or without other cognitive issues, and non-amnestic (non-aMCI), marked by impairments in cognitive areas other than memory (61).

2.2.3 Brain structural and functional changes in typical aging vs in MCI

Typical aging and MCI manifest distinct structural and functional changes in the brain, which impact cognitive functions, with notable variations in the extent and regions affected. Aging results in changes in brain function and structures (73), potentially affecting cognitive abilities. Typical cognitive aging causes a decrease in overall brain volume, as well as in grey and white matter. The most significant atrophy occurs in the prefrontal cortex, with a moderate reduction in the temporal lobes, mainly due to changes in grey and white matter structures (73,74). Functional studies of normal aging suggest a decline in metabolic activity in the prefrontal cortex and a decrease in connectivity and network integrity, resulting in cognitive changes in older adults (73,74). Conversely, in MCI, structural brain changes are larger compared to normal aging. Magnetic Resonance Imaging studies reported a larger volumetric reduction in the medial temporal lobe in MCI compared to normal aging (75). Functional studies of MCI showed disruptions in brain activity, involving various parts of the brain, including the prefrontal, posterior cingulate, and parietal cortices (76)

2.2.4 Cognitive changes associated with typical aging VS MCI

Cognitive changes observed in typical aging and MCI differ significantly. In this section the changes of each cognitive domain in typical cognitive aging vs MCI will be discussed. Processing speed, a key indicator of cognitive performance, declines with aging (74), and this reduction is more noticeable in People with MCI (PwMCI) (77). Research indicated that in addition to potential deceleration of processing speed in simple tasks, PwMCI might also encounter significant delays in their reaction times, which are crucial for ensuring safe, appropriate, and efficient interactions within their environments in everyday life (78).

Attention declines with normal aging, especially during multitasking (46). However, PwMCI experience more significant attention deficits compared to typical aging (79) in both simple and complex sustained attention and divided attention, suggesting a higher risk of developing dementia (80). The attention deficits in MCI, along with memory and executive function issues, exacerbate difficulties in managing complex tasks such as financial management, learning, and daily routines (81,82). Sensory memory declines with aging (83,84). PwMCI show a significant reduction in sensory memory compared to people with typical cognitive aging (85). These sensory memory issues can make the effortful sensory tasks challenging. For example, listening in noisy environments becomes difficult due to impaired encoding of the stimulus details, making it harder to process and understand speech. This decline affects the ability to retain and integrate fine-grained auditory information, which is crucial for effective communication in complex listening situation (83). PwMCI might also experience difficulties in visual searching tasks (86) which is related to deficits in their sensory memory. Additionally, STM typically declines with age (87). However, this decline is more pronounced in PwMCI who show significant deficits in both visual and visuospatial STM compared to healthy older adults. These impairments can significantly impact the ability to perform everyday tasks that require learning and retention of information (86).

Moreover, in typical aging, WM decline may manifest as slower processing speeds and reduced capacity to hold and manipulate information temporarily, affecting tasks that require multitasking or complex problem-solving. These changes, while noticeable, generally do not severely impact daily functioning (56). However, WM deficits are one of the most common impairments in MCI, affecting everyday tasks that require sustained mental effort and organization, such as managing finances, following multi-step instructions, and maintaining medication schedules (88,89). In particular, environmental distractors have a disproportionate effect on the WM performance of PwMCI, making it challenging for them to handle tasks that require attentional control and the ability to manage distractions and interruptions. As a result, PwMCI often experience greater susceptibility to memory-related deficits, leading to difficulties in daily functioning and increased vulnerability to developing dementia (88).

In terms of LTM, episodic memory typically declines with aging (90), and this decline is more noticeable in PwMCI than what is expected from typical aging (70). Research shows that PwMCI exhibit significant deficits in tasks requiring the recall of spatial locations and item recognition, reflecting an impairment in episodic memory. These deficits can affect daily activities that rely on recalling recent events or navigating familiar environments (91). In contrast, semantic memory which handles general knowledge learned during life (53) generally remains stable with age (92). However, it declines in PwMCI. This is particularly evident in tasks involving the naming of famous people or recalling factual information, indicating that MCI impacts not only episodic but also person-specific semantic knowledge (91). In contrast to declarative memory, procedural memory and emotional memory remains stable across the lifespan (93) and in MCI (94,95).

Regarding visuospatial skills, basic abilities generally remain intact with normal aging, thought older adults may experience slower processing speeds. In contrast, advanced skills, such as visuospatial memory and mental imagery, typically decline as part of aging process (55). MCI is associated with further impairment in visuospatial skills beyond what is expected from normal aging (55). PwMCI often show deficits in spatial short-term memory, spatial orientation, and the ability to construct and manipulate spatial representations. These impairments can significantly affect daily activities, such as navigating new environments, remembering the locations of objects, and interpreting complex visual information (55). The decline in visuospatial abilities in MCI can also impact more complex tasks that require the integration of spatial and executive functions, leading to increased difficulty in planning and executing tasks that involve spatial components. For example, individuals with MCI may find it challenging to follow directions, assemble objects, or perform tasks that require an understanding of spatial relationships, which can affect their overall quality of life (55).

Executive functions, including both inhibitory control and cognitive flexibility declines with normal aging (56,74). This decline is more evident in PwMCI, potentially impacting effortful daily routines (96,97). Inhibitory control, the ability to suppress irrelevant stimuli or responses, and cognitive flexibility, the capacity to switch between different tasks or mental states, are essential for effective executive functioning. In people with MCI, deficits in these areas are common and can predict a worse prognosis. These impairments interfere with the ability to organize and process information, resist distractions, and implement strategies for encoding and recall, affecting everyday routines such as managing finances, medication adherence, and other complex tasks. The impairment in executive functions is a marker of potential progression to Alzheimer's disease, making early identification and intervention crucial (97).

Language skills generally remain stable with aging (98). However, specific abilities like naming and verbal fluency might decline with age (99,100). MCI is also linked to subtle language deterioration, signaling a potential progression to dementia (98,100,101) . This deterioration includes issues with word retrieval, reduced speech fluency, and changes in syntactic complexity.

Although these language impairments are less severe than those observed in Alzheimer's disease, they are significant enough to impact daily communication (101).

2.2.5 MCI diagnosis

Early detection of MCI is beneficial for several reasons. It facilitates timely access to information and treatments (9). It also allows for the modification of risk factors like smoking, physical inactivity, and social isolation, potentially delaying disease progression (11). Additionally, it assists in identifying potential participants for research, essential for evaluating new treatments (9,12). Early detection enables patients to converse with clinicians and family members about their condition, providing insights into prognosis, care preferences, and future financial planning. (9,10). However, diagnosing MCI is challenging and cannot be confirmed by a single test. People who are concerned about their cognitive abilities should be thoroughly assessed through a detailed history and clinical examination. This evaluation should emphasize cognitive capabilities, everyday functional status, current medications, and any neurological or psychiatric conditions. It is also important to conduct laboratory tests (13). The main aims are to distinguish MCI from typical aging or dementia and to detect any reversible factors contributing to MCI, such as depression, side effects from medications, thyroid issues, or deficiencies in vitamin B12 or folate (13). Cognitive function is assessed using traditional cognitive tests such as the Montreal Cognitive Assessment (MoCA), Mini-Mental State Exam (MMSE), Saint Louis University Mental Status (SLUMS), and Quick mild cognitive impairment (Quickmci).

The MMSE is one of the most used cognitive tests measure several cognitive abilities in 5 to 10 minutes. MMSE was shown to have a good test-retest reliability (0.80–0.95) (102–104). MMSE is also concurrently valid (103,104); however, it is not sensitive enough to detect MCI. Sensitivity and specificity have been recorded inconsistently ranging from 13% to 97%, and 60%

to 100% respectively, considering this variation in accuracy, MMSE is less reliable for MCI detection, specifically at an early stage (105–108).

The MoCA is one of the most common paper-based cognitive tests that evaluate short-term memory, visuospatial skills, executive function, attention, concentration, working memory, language, and orientation within 10-15 minutes (16). The MoCA demonstrates high test-retest reliability, good internal consistency, as well as strong concurrent and construct validity (109). Content validity is also supported by a high correlation between MoCA and MMSE scores (16). Sensitivity and specificity vary depending on the cut-off points used, with reported sensitivity ranging from 67% to 100% and specificity from 50% to 95% (108). Research also suggested 89% sensitivity and 79% specificity for MCI detection, with the cutoff point of 26 for MCI and 18 for dementia (110). The AUC for MoCA is 0.84 in differentiating MCI from controls. The MoCA is also adjusted for educational level (16). Despite its advantages, the MoCA has some limitations including educational bias for low level of education, associated cost for usage, and the requirement for administrator training (108) .

The SLUMS is a cognitive screening tool that can be administered in less than 10 min to assess attention, immediate recall, orientation, delayed recall, calculation, visuospatial abilities, and executive functions (18). However, the SLUMS is less accurate for MCI detection compared to the MoCA, with sensitivity ranging from 73% to 95% and specificity ranging from 65% to 81%, with education adjustment (111). Regarding psychometric properties, although the existing literature offers initial support for the SLUMS, further research is necessary to assess its reliability, validity, and application across more diverse populations (111).

The Qmci is a brief paper-based cognitive test designed to differentiate between normal cognitive function, subjective cognitive disorders, MCI, and early dementia. It assesses orientation, memory, language, visuospatial skills, and executive function in 3-5 minutes. The Qmci demonstrates good test-retest reliability and validity (112–114). With a cut-off point <62, for MCI detection, it achieves a sensitivity of 90% and specificity of 87%, and the AUC for differentiating MCI form controls is 91% (115). Compared to the MoCA, the Qmci's primary advantage is its brevity, requiring only half the time to complete while offering greater accuracy for MCI detection (115,116). Additionally, the Qmci provides different cut-off points according to both age and educational level (117).

2.2.6 Advantages and disadvantages of cognitive tests

The cognitive tests can distinguish cognitive impairment from normal aging and specify and quantify the area of impairment (19). They are widely recognized in clinical practice for their proven psychometric properties (118). Moreover, they are often administered in paper-and-pencil format, which is straightforward and familiar for older adults. Despite the merits, cognitive tests have some limitations. Scoring can be subjective, leading to potential human errors and affecting test accuracy (20). These tests often fail to represent the complexity of real-life tasks (21). Moreover, the need for trained clinicians to administer the test restricts access, making continuous monitoring of cognitive changes difficult and costly (22,23). Traditional cognitive tests could induce state anxiety, an "in-the-moment" measure of anxiety as described subjectively by an individual, in older adults (24,119), potentially leading to test avoidance or negatively affecting their cognitive performance (25). The tests could be perceived as a threat (120), particularly among older adults who may have concerns about their cognitive health and the implications of receiving a low score. Such concerns could include potential changes in their living arrangements or decreased autonomy. This anxiety might divert attention toward the threat, therefore reducing cognitive performance during the tests (120) and leading to potential misinterpretation of results and implications for MCI screening.

Therefore, the need for alternative screening methods for MCI arises from several limitations associated with current cognitive tests. These tests, while beneficial, often fail to capture the subtle changes in cognitive functioning that characterize MCI. The variability in sensitivity and specificity across different tests and populations highlights the difficulty in achieving an accurate MCI screening. Furthermore, issues such as educational bias, costs, the need for trained administrators, and the potential for inducing anxiety in test-takers can significantly impact the efficacy and accessibility of these tools. Additionally, this limitation makes it challenging and costly to track the cognitive changes over time (22,23). Research also has highlighted a significant limitation of current neuropsychological assessments, which is their administration at widely spaced time intervals (26). Such infrequent testing is susceptible to being affected by factors such as motivation, mood, stress or fatigue level.

2.2.7 Summary and gaps

Cognitive tests are valued in clinical practice for distinguishing cognitive impairment from typical aging and quantifying specific impairments due to their proven psychometric properties. These tests, typically in a familiar paper-and-pencil format, are straightforward for older adults (108,118). However, they have limitations such as subjective scoring errors (20), failure to represent real-life task complexity (21), the need for trained administrators, and inducing state anxiety in older adults (24), which can affect test performance, interpretation of the results, and older adults' reluctance to be monitored regularly. While beneficial, these tests often fail to capture the subtle changes in cognitive functioning that characterize MCI. The variability in sensitivity and specificity across different tests and populations highlights the difficulty in achieving accurate MCI screening (108). Issues such as educational bias, costs, the need for trained administrators, and the potential for inducing anxiety in test-takers can significantly impact the efficacy and accessibility of these tools (108). Furthermore, the infrequent administration of neuropsychological assessments is a significant limitation, as it is susceptible to factors such as motivation, mood, stress, or fatigue level.

To address these challenges, there is a compelling need to explore and develop innovative screening tools that are more accessible, cost-effective, and sensitive to the early stages of cognitive decline. Additionally, investigating new methods for regular MCI screening that could reduce state anxiety among older adults is essential, as this might enhance their willingness to engage in consistent monitoring.

2.3 Digital technology for MCI screening

2.3.1 Digital technologies

Digital technologies offer innovative solutions for screening MCI. These tools provide continuous, real-time data collection, facilitating early detection and intervention (9). Digital technologies encompass variable types, including wearable devices, home-based monitoring system, in-car sensors, AI, Mobile apps, VR systems and SCGs.

Wearable devices include sensors and trackers that monitor physical activity, sleep patterns, and other physiological data (26). For instance, accelerometers and GPS-enabled devices can provide insights into a patient's mobility and spatial navigation, which are indicators of cognitive functions (26) Home-based monitoring systems involve the use of embedded sensors in the home environment to continuously collect data on daily activities. Technologies such as infrared motion sensors and magnetic contact door sensors can unobtrusively monitor changes in a person's routine, which may indicate cognitive decline (26) In-car sensors are embedded devices within vehicles that monitor driving behavior and vehicle performance. These sensors can track metrics such as speed, braking patterns, and navigation routes. For MCI detection, in-car sensors can provide valuable data on a driver's cognitive functions by analyzing deviations from normal driving behavior, which may indicate cognitive impairment. Monitoring these behaviors over time can help identify early signs of MCI, allowing for timely interventions and support (9,26).

AI refers to the development of computer systems capable of performing tasks that typically require human intelligence, such as learning, reasoning, and problem-solving. In the context of MCI detection, AI algorithms can analyze large datasets from various sources, including wearable devices and electronic health records, to identify patterns indicative of cognitive decline. AI can also enhance the accuracy and efficiency of diagnostic tools by providing real-time analysis and predictive insights, helping clinicians make more informed decisions about patient care (9).

Mobile/computer/tablet-based apps and software provide a wide range of functionalities. In healthcare, apps and software are increasingly used for monitoring health conditions, managing treatments, and providing telehealth services. For MCI detection, the apps and games can administer a digital version of traditional cognitive tests, track daily activities, and collect self-reported data from users (9,26,27) . These apps offer a convenient and accessible way for continuous cognitive monitoring, enabling early detection and management of cognitive decline through user-friendly interfaces and real-time feedback (26).

VR technology creates immersive, computer-generated environments that can simulate real or imagined worlds. In healthcare, VR is used for therapeutic purposes, such as pain management, physical therapy, and cognitive rehabilitation. For MCI detection, VR can provide a controlled environment to assess cognitive functions through tasks that mimic real-life activities, such as navigating virtual spaces or performing complex tasks. This immersive approach allows for a detailed evaluation of a patient's cognitive abilities in a safe and engaging manner (9,26). Finally, SCGs for screening MCI offer several key advantages over other digital technologies. SCGs are highly accessible and cost-effective, making them suitable for a wide range of users, including those in remote or underserved areas. They provide an enjoyable and engaging experience, which helps to maintain user motivation and reduces the anxiety often associated with traditional cognitive tests. Additionally, SCGs might be more familiar to older adults compared to other high-tech solutions, making them easier to be adopted and used. Furthermore, SCGs do not require very complex algorithms to analyze the data compared to AI, allowing for straightforward implementation and interpretation of the results. These factors combined make SCGs a practical and effective tool for early detection of cognitive decline in older adults.

2.3.2 Digital biomarkers

Digital biomarkers are characterized as objective, measurable physiological and behavioral data collected via the digital technologies, offering valuable insights into various health-related outcomes (26). Digital biomarkers can be collected through several technologies. The real-time and continuous data gained from digital biomarkers could facilitate cognitive screening both in clinical settings and through home-based methods (9). Digital biomarkers have demonstrated significant differences in cognitive outcomes related to memory and executive functions between older adults with cognitive impairments and their healthy counterparts (27). They potentially serve as sensitive indicators for MCI and dementia. With diagnostic performance comparable to traditional paper-and-pencil tests, digital cognitive biomarkers are an effective and promising proxy for the clinical detection of MCI (27).

2.3.3 Serious Computer Games and their classification

Given that the purpose of this proposal is to examine an SCG, G3, for MCI detection, the literature review will focus on SCG technologies. SCGs are fully-fledged games designed for purposes beyond entertainment (31). The integration of digital technologies with the capabilities of data tracking (9) and the growing positive attitude toward video games among older adults (32) make SCGs a promising tool for cognitive screening in older adults. In the context of SCGs, digital biomarkers are captured through the game's interaction with the player. These markers can include various metrics, such as reaction time, playing time, number of errors, and final game score (40).

SCGs can be classified into two categories: hardcore and Casual Video Games (CVGs). Hardcore games are complex, demanding high commitments, and prolonged playtime, while CVGs are simpler, requiring low commitments. The rules, goals, and required actions in CVGs are also more straightforward (121). Older adults often find it challenging and discouraging to learn and play fast-paced hardcore video games, especially those containing violent content (122–124). In contrast, the features of CVGs, which remove any possible barrier to someone enjoying the game, are considered more suitable and user-friendly for seniors (125). These simple games with clear rules also have the potential to serve as a joyful activity for older adults' rehabilitation ranging from prevention, and assessment to intervention.

Understanding the different types of CVGs is important for designing more enjoyable games and catering to player preferences (121,126). Research also suggest that different games involve various cognitive and physical abilities (39,125,126). Therefore, implementing proper games can increase the likeability and usability of the games, particularly for older adults with cognitive decline. Based on engaged cognitive abilities and required interactions, rules, and goals CVGs can be classified into casual action, casual puzzle, casual simulation, and casual strategy games (121).

Casual action games, exemplified by the Whack-a-Mole, require a simple series of actions and usually involve eye-hand coordination and fast reactions (121). Causal puzzle games are characterized by straightforward challenges such as matching, sorting, or solving puzzles, requiring reasoning, and problem-solving skills (121). Casual simulation games simplify real-world activities (e.g., sports, cooking, driving) without the complexities of hardcore games, involving context-related knowledge, cognitive coordination, information processing, and movement control (121). Casual strategy games, for example, Tower Defense, require strategic decision-making, planning, and the ability to modify actions to achieve a goal but with a more accessible and less complex approach than hardcore strategy games (121).

Research indicated that CVGs with any type are usable for seniors (121), in particular, casual simulation games were found to be more comprehensible for older adults (125). Therefore, a simple game with clear rules that simulates a real environment, and familiar scenarios could be enjoyable and engaging for older adults, especially those with cognitive decline.

2.3.4 The advantages and disadvantages of Serious Computer Games compared to traditional cognitive tests

SCGs present several benefits compared to traditional cognitive screening methods which typically involve paper-and-pencil tests. SCGs offer consistent and standardized administration procedures, reducing rater bias (27). The standard procedures ensure precise control over the presentation of stimuli and enable accurate measurements. This level of precision could explain why many game-based screenings show comparable or better diagnostic performance compared to traditional tests (27).

Another significant advantage of SCGs is their accessibility, even for people living in remote areas (37), which also facilitates the recruitment of large sample sizes for research purposes. In contrast, the administration of traditional cognitive tests often requires trained clinicians, limiting access for older adults who live in remote areas. This limitation makes it challenging and costly to monitor cognitive changes over time (22,23).

SCGs also offer the potential advantages of adaptability and customization for screening different cognitive domains (127), which can improve user motivation and acceptance (128).The difficulty and features of SCGs could be adjusted dynamically based on the player's performance, needs, and preferences (128,129). This contrasts with traditional tests that often offer inflexible formats. However, more research is needed to explore the full potential of this adaptability and customization (129).

SCGs can also incorporate ADL and iADL within the game scenarios (27), offering a more realistic measurement of cognitive abilities and reflecting how impairments might affect everyday tasks (130,131). The home-based and self-administered aspects combined with ADL and iADL simulation, enhances the ecological validity of SCGs compared to traditional tests administered in clinical settings, which often lack real-life components (132).

Moreover, SCGs provide an engaging and enjoyable experience, potentially reducing the anxiety often induced by traditional tests in older adults (24). Research suggested that using video games could cut the influence of the white coat effect, the anxiety resulted from being assessed by a health care professional (133) and the overwhelming feeling associated with traditional screening methods (118). The stress-relieving benefits of video games have been also reported by older adults who play them (32). However, no research has been done to examine the different levels of anxiety among older adults with and without cognitive impairments while doing the traditional tests and playing an SCG.

Despite the advantages, SCGs present several limitations. A primary concern is the reluctance of many older adults to engage with new technological devices (134) and potential of experiencing technology anxiety among older adults, making the application of SCGs challenging (135). In contrast, older adults might be more familiar with the process of performing traditional tests. Additionally, SCGs have not been integrated into standard clinical practice (135), partly due to the lack of a set of standardized guidelines and normative data that are necessary for clinical interpretation (133). However, traditional tests have well-established psychometric properties and are commonly used in clinical practice (118).

Moreover, unlike traditional tests, the SCGs are still in the early stages of consideration for clinical practice (134); and the feasibility of using different SCGs has not been comprehensively examined (136). However, traditional tests have been recommended for clinical practice (137). Research on SCGs for older adults often excludes individuals with uncorrected vision and hearing impairments (23,34,44), raising concerns about the generalizability of results. However, established cognitive tests like the MoCA offer adjusted versions for such individuals (138). Another limitation is the lack of regulations regarding the commercialization of SCGs for older adults, potentially causing safety issues. Companies should comply with approved rules to ensure that the games are safe and useful for targeted populations (135), especially since older adults might play these games at home without clinical supervision (127). Finally, the need for internet access to play SCGs can be a barrier for older adults with limited internet connectivity (127), affecting their inclusivity.

2.3.5 Serious Computer Games as screening tools for MCI

Only a handful of studies have applied SCGs for MCI screening, revealing significant differences in game performance between older adults with MCI and their healthy counterparts For instance, Zygouris et al. noted that individuals with MCI took significantly longer to complete games than their healthy counterparts ($t = 4.84$, $p < 0.001$) (139). Similarly, Gielis et al. observed distinct differences in 12 out of 23 digital biomarkers, including time-based, error-based, and result-based metrics, highlighting substantial discrepancies between the two groups (140). Therefore, the SCGs could differentiate or classify older adults with and without MCI. However, more studies are needed to test more game scenarios and investigate the association of demographic factors with game performance in PwMCI and healthy counterparts.

Research has also explored the criterion validity of the game-based screenings for MCI detection, highlighting significant correlations between game metrics and cognitive status (39,41,139–146). Numerous game metrics, including completion ability, gameplay duration, accuracy of actions, and total score, have been examined for their relationship with cognitive status. For instance, Zygouris et al. found a negative correlation ($r= -0.2$) between game playtime and cognitive test scores, suggesting that older adults with lower cognitive status required more time to complete games (139). Zygouris et al. also found correlations between education ($r= -0.3$ and $r= -0.23$) and age ($r= 0.2$ and $r= 0.24$) with the total time needed to complete the game (22,139). It means that a higher education level is associated with faster game completion, while older age correlates with longer completion times. Cabinio et al. found a correlation between game performance accuracy, reaction time, total playing score and cognitive status in PwMCI and the comparison group (43). Although these findings affirm the criterion validity of game-based screenings, the correlations are not strong. Only one study explored the correlation of the demographic variables and the game performance. Further research is necessary to clarify the relationships between traditional cognitive screening scores and various game metrics, evaluating the validity of game-based screenings.

Only one study has investigated the reliability of game-based cognitive screenings, indicating a significant gap in the research. The researchers conducted a test-retest reliability study and found moderate reliability in their assessments (146). This study had a very small sample size of only nine healthy controls, which is insufficient to draw robust conclusions. To establish the reliability of game-based cognitive screenings, more extensive research with larger and more diverse samples is necessary.

Research showed that the game-based screenings could classify participants into two groups, with typical cognitive aging and PwMCI (34,41,139,140,143,144,147) Moreover, the diagnostic accuracy of game-based screenings, assessed through metrics like sensitivity, specificity, and Receiver Operating Characteristic (ROC) curves, have surpassed traditional paper-and-pencil tests (140,144,146). In addition, the diagnostic accuracy of a SCG, the Smart Aging Serious Game (SASG), was investigated by using two classification models, Random Forest (RF) and logistic regression (LR) (34). Both models used the same variables as potential predictors, including traditional cognitive tests and SASG total scores. The RF analysis resulted in a 75% accuracy rate for the healthy comparison group versus MCI classification. Moreover, the LR analysis resulted in an 87% accuracy rate for the classification of PwMCI versus the healthy comparison group (34). Despite these encouraging results, the sample sizes in these studies need to be larger to conclude generalizable results. Moreover, the variation in game scenarios, features, and metrics used across studies prevents drawing a conclusive statement that would apply to all SCGs.

The predictive validity of game-based screenings has also been explored. Several studies provided valuable insights into the use of game-based screenings for examining cognitive status in older adults. These studies explored the predictability of such screenings, particularly focusing on Positive Predictive Value (PPV) and Negative Predictive Value (NPV), critical measures for evaluating the responsiveness of diagnostic tests (39,143,144). PPV of the game-based used by Valladares-Rodriguez et al. was reported as 90% (143). However, PPV reported by Bonnechère et al. and Chua et al. were 24% and 66.7% respectively (39,144). Using different games, sample sizes, and demographic variables might explain this inconsistency. Therefore, more studies with larger sample sizes are needed in this area. Moreover, the incorporation of demographic information as predictors in models analyzing the diagnostic accuracy and predictability of SCGs remains unexplored, indicating another area for future research.

The psychological conditions such as anxiety of MCI screening I n older adults have been less explored. Only one study showed that doing traditional cognitive screening might be considered a threat for older adults, potentially generating anxiety (148). The potential of game-based screenings to provide an anxiety-free environment has not been directly compared to traditional cognitive screenings, highlighting a gap in current research.

Research on game-based screenings has varied widely in terms of the game scenarios employed. Some studies utilized games that closely mimic real-life activities, such as the Virtual Super Market (44,139,141,146,149), SASG (34,43,145), and Virtual Action Planning Museum (41). These games are designed to simulate daily tasks and challenges, potentially providing a realistic measure of an individual's cognitive abilities related to ADL and iADL. Conversely, other studies have opted for simpler game scenarios that may not fully capture the complexities of ADL and iADL, such as Klondike solitaire (140), Whack-a-Mole (23), and short mobile games

(147). These games often lack the depth required to assess the range of cognitive skills such as planning, problem-solving, attention, and memory, which are critical for independent living. The importance of assessing a broad array of cognitive abilities needed for the independent execution of iADL has been underscored (131). The responsiveness of SCGs in assessing cognitive performance in older adults is significantly enhanced when the games incorporate realistic ADL or iADL scenarios. Therefore, there is a need for further research into SCGs that mimic real-life scenarios. Such games are particularly crucial for effectively screening for MCI among older adults.

Two primary methodologies are employed for using SCGs in game-based cognitive screenings: analyzing data from existing games, and creating custom games that mimic traditional cognitive assessments, ADL, or iADL specifically for older adults. For instance, the Microsoft Solitaire Collection was enhanced with tools to measure digital biomarkers such as the time taken to make decisions and in-game errors, potentially reflecting changes in planning, executive function, or attention (140). Similarly, a variety of games, including Sudoku, Word Search, and Whack-a-Mole were employed to measure digital biomarkers, game metrics, such as reaction time, error count, and correct actions, which might indicate processing speed, attention, and memory (23,40,150). Additionally, a set of seven brain-training mini-games within the Peak mobile app were used for assessing cognitive status in older adults. Different game metrics were collected, including total time of playing and total score, which involved memory, processing speed, attention, visuospatial skills, and language (147). Although these popular games are engaging and have been shown to correlate with cognitive health, they often fail to cover all cognitive domains essential for comprehensive cognitive screening instruments. In addition, some of them were not specifically tailored to the needs of older adults, including considerations for age-related changes.

In contrast, research into custom-designed games has shown promising directions. Several studies employed a bespoke SCG, virtual supermarket, for cognitive status detection, using game metrics such as time duration, correct items, bought unlisted items, correct quantities, and correct money, which involved visual and verbal memory, executive function, attention, and spatial navigation, with the emphasis is on the execute function (44,139,141,146,149) . Additionally, the SASG was utilized, specifically aimed at the early detection and prevention of cognitive impairments in older adults (34,43).They explored several game metrics, including performance accuracy, reaction times, and total game score, which involved memory, attention, executive functions, working memory, and visual-spatial processes (34,43). These custom-designed games are tailored to address the unique cognitive needs of this population.

These efforts in employing commercial and custom-designed games for cognitive evaluation have shown promising outcomes. Nonetheless, the field requires further investigation to establish strong, conclusive findings on their diagnostic accuracy and validity.

In terms of usability, only two previous studies have investigated the usability of game-based screenings for MCI detection (43,44). These studies demonstrated that the usability of their game-based screenings was good. Both games used touch screens and simulated daily routines (43,44). However, the usability of SCGs using other delivery modes, such as computers and mice, has never been explored. Furthermore, the usability of SCGs is highly dependent on the specific game and its features, necessitating the assessment of different SCGs to confirm their usability by older adults. Despite these findings, there is a lack of studies addressing all diagnostic accuracy, validity, and usability. Usability is crucial for the adoption of SCGs as cognitive screening tools, as it directly impacts the effectiveness and reliability of the screenings. Therefore, it is essential to evaluate the usability of different SCGs comprehensively to ensure they can be effectively used by older adults in various formats.

The availability of SCGs varies significantly, with several factors impacting their accessibility for broader use, including being available in several languages and being commercially available for free. Many SCGs tested for MCI detection are designed primarily for research purposes and are not always widely available for public use. Some of the SCGs support multiple languages to accommodate diverse populations, as seen in studies where games were implemented in English, Korean, and Italian, Greek, Turkish, Korean, and Chinese. However, the applied SCGs are not accessible for people communicating in other languages. Some SCGs used in previous studies (41,43,44,144) are also available on common platforms such as tablets and computers for research, but they may not be accessible outside of controlled research settings. This limited availability can pose a challenge for widespread implementation and underscores the need for further development and commercialization to make these tools more accessible for clinical use and everyday settings.

2.3.6 Summary and gaps

In conclusion, various studies have applied SCGs for MCI screening among older adults, revealing significant differences in game performance between those with MCI and their healthy counterparts However, despite these promising findings, several gaps and areas for further study remain evident. Notably, the correlations between the game metrics and the traditional cognitive scores found were not robust, and demographic variables were often overlooked in these analyses, limiting the concurrent validity of the used game-based screenings. This oversight suggests a need for more comprehensive research to understand better how demographic factors might influence the outcomes of game-based cognitive screenings.

The variability in game scenarios, dependence of the results and usability on the specific games and their availability, and small sample sizes also limit the generalizability of these findings, highlighting a clear need for further research. Future studies should also focus on integrating demographic variables, employing larger sample sizes, and exploring a wider variety of game types to enhance validity and usefulness of SCGs. Furthermore, the availability of SCGs used in previous studies is limited, and they are not accessible for older adults and clinicians to use in everyday life or clinical settings.

Research should also examine the psychological impact of game-based screenings, such as state anxiety, compared to traditional screenings. Understanding the levels of anxiety induced by different types of screenings can help improve the design and implementation of SCGs, making them more user-friendly and less intimidating for older adults. This could broaden the acceptance and effectiveness of these innovative tools in MCI screening.

Moreover, there is a need to explore the integration of real-life scenarios into SCGs, such as Activities of Daily Living (ADL) and instrumental ADL (iADL), to provide a more realistic assessment of cognitive abilities. Custom-designed games that mimic real-life activities have shown promising results, and further research in this area could enhance the ecological validity of SCGs.

In conclusion, while SCGs hold great promise for MCI screening, addressing these gaps through comprehensive research will be essential for establishing their reliability, validity, generalizability and widespread applicability.

3. Method

3.1 Study design

This study is an observational cross-sectional study. Since the G3 in this study has never been used for screening cognitive status, its validity as an indicator for MCI and its diagnostic accuracy are unknown. Given the novelty and untested nature of G3, a cross-sectional design is chosen for its cost-effectiveness and time efficiency, making it suitable for a feasibility study to explore the game's validity, usability, and diagnostic accuracy. Moreover, recruiting a large sample size for a longitudinal or repeated measures study and undertaking extensive data collection would be unethical for a tool whose usability, validity, and diagnostic accuracy have not been previously assessed. This is particularly relevant for older adults with cognitive impairments, who are a vulnerable population. Therefore, a cross-sectional study is the best approach for the first steps of research in the area using the G3.

3.2 Participants

3.2.1 Inclusion criteria

- Older adults who are aged 65 and above with typical cognition or MCI as reported by themselves, or a health care professional.
- Older adults participating in this study must have MoCA score of 18 or higher.
- Older adults participating in the study must have functional vision and hearing, with or without aids such as glasses or hearing aids that enable them to interact with the game and comprehend the instructions. As part of the study recruitment activities, the researcher will explain the tasks required and discuss the vision and hearing demands.

- Older adults participating in the study must be capable of communicating and comprehending assessments, instructions, and simple sentences in English, as communication and comprehension is essential for interacting effectively with game components and the researcher. To assess their communication, reading, and comprehension skills, the researcher will provide participants with a few sentences in English related to the game content. Participants will be asked to read these sentences aloud and explain the meaning of the sentence to confirm their ability to read and understand the content.
- Older adults participating in the study must have adequate upper extremity function to play the game, using a mouse and do paper-and-pencil based measurements, using a pencil. During the study's introduction and training part of the game, potential participants can report any physical limitations. The researcher will also screen for these issues.

3.2.2 Exclusion criteria

- Older adults currently suffering from Influenza, COVID-19, or any other viral illness at the time of data collection that could impair their performance will be excluded. These conditions could impair their performance, potentially affecting the reliability of the outcomes. Additionally, the presence of such illnesses could pose a health risk to other participants who use the same equipment, as well as to the researcher.

3.3 Sample size

The correlational analysis was selected for determining the sample size of this study. The main reason for that is that the diagnostic accuracy and validity testing are the primary objectives of this project. Calculating the sample size based on correlational analysis offers a robust approach to examining the relationship between game performance and cognitive status, requiring a moderate number of participants. Thus, this study, designed with a statistical power of 0.8, an alpha level of 0.05, and a medium effect size of 0.7, requires a minimum sample size of 58 participants. Twenty-nine older adults (65 and above) who meet the diagnostic criteria for MCI, and 29 older adults with typical cognition will be eligible to participate in the study.

Other reasons for justifying the sample size include: 1) The statistical analyses to answer questions that aim to compare two conditions, or two groups requires a smaller sample size; and this small sample size is insufficient to justify correlational analysis. 2) the "Events Per Variable" (EPV) rule is often used in statistical modeling, particularly in logistic regression, to determine the minimum sample size needed to ensure reliable and valid results. The general rule is to have at least 10 events (outcomes of interest) for each predictor variable (151). Therefore, using regression analysis to explore the six associated factors (game performance, age, sex, educational level, tech savviness, and living status) with the presence of MCI would necessitate 60 events (instances of the outcome of interest). Assuming an equal distribution of events and non-events, at least 120 participants would be needed in total to achieve 60 events, ensuring that each predictor variable is adequately supported by the data and enhancing the reliability of the statistical model. However, for a feasibility study involving a brand-new, untested test, it is not ethical to recruit a large sample size and burden vulnerable older adults with participation. Besides, at this point of the study, it is not known how many independent variables will be included in the model and that depends on the results of the factorial analysis that precedes the logistic model. Therefore, I aim to treat the research about the associated factors with the presence of MCI (RQ4) as a pilot to gather preliminary data. This approach can help refine the research design and hypotheses, and the results can be used to justify the need for a larger study in the future. Additionally, based on the data, a simpler model with only the strongest predictors will be used to produce a more reliable regression model. Thus, for an initial study on a new test, correlational analysis is the most practical choice, allowing us to assess concurrent validity without requiring an excessively large sample size.

3.4 Sampling strategy

The accessible population of older adults with MCI and typical cognition.

3.5 Settings and Materials

3.5.1 Settings

The study will be conducted either in the spaces provided by the partner community organizations (e.g. assistive living facilities) or in Room 1-43 or 1-45 of the Corbett Hall, at the Faculty of Rehabilitation Medicine, University of Alberta.

3.5.2 Materials

A 13-inch Dell Latitude 5411 laptop, equipped with an Intel(R) Core (TM) i7-10850H CPU, 16 GB RAM, and a Microsoft mouse, customized for both left and right-handed individuals, will be used to play the game. The game G3, will be utilized for the game-based screening.

G3 was designed to simulate grocery shopping, aiming at challenging cognitive skills in a fun and engaging way. Originally developed in Edmonton, Alberta, by Glenrose Rehabilitation Research, Innovation & Technology (GRRIT), the game was created in collaboration with occupational therapists to meet the specific needs of older adults. G3 consists of 50 stages and was initially intended for cognitive training. However, in this study, it will be tested for the first time as a cognitive screening tool.

The game features stages with varying difficulty levels (easy, normal, hard), based on the number of items in the shopping list, according to needed ingredients for a meal. For this study, six stages will be selected for participants to play. Players take a virtual trip to the grocery store to shop for ingredients of a virtual dinner for celebrity guests. Participants can choose their player character, and the inclusion of old-time celebrities as non-player characters, along with short written conversations with these celebrities, aims to create a sense of belonging for older adults. In some stages the guests may ask for a change in the shopping list, for example because of an allergy, that need to be considered by the player.

G3's design includes several features to enhance its appeal and effectiveness for older adults. Using a familiar scenario like shopping increases the ecological validity of the game. The option to select a male or female older adult character helps develop a sense of belonging, while the ability to pause and start the game easily improves the sense of autonomy. The goal of the game is straightforward, making the instructions easy to understand. The difficulty levels are aligned with the abilities of most older adults, ensuring that the game is challenging yet accessible.

The original game was designed for a large touchscreen measuring 24 inches by 80 inches. GRRIT collaborated with two companies, Rebel Parachute and Beach & Lanes, to transform the game into an app for iOS and Android tablets. The game was redesigned to fit smaller screens and various tablet shapes for a free commercial version of G3. However, for this study, a computer-based version that can automatically record game metrics will be used.

3.6 Variables

The study variables are the following:

- Game performance collected through various game metrics, including total time of playing, the ability to complete the whole game, the ability to manage the budget, number of errors, the number of checking the shopping list, and the game performance accuracy.
    - Total Time of playing: This numerical variable refers to the total time that takes to complete all 6 stages in seconds with the maximum of 1800 seconds.
    - The ability to complete the game: This binary variable (1= Could complete, 0= Could not complete) refers to the participant's ability to complete all the 6 stages of the game.
    - The ability to manage the budget: This binary variable (1 = Could manage, 0 = Could not manage) refers to the participant's ability to keep their purchases equal to or below the budget limit provided for each level.
    - The number of errors: This numerical variable refers to the total number of mistakes made by participants, including mistaken, missed, and repeated items purchased.
    - The number of times the participant opens up the reading list: This numerical variable refers to the total number of times the participant open and check the shopping list within the 6 stages.
    - The game accuracy: This numerical variable represents the success in the game, ranging from 0 to 100, where higher values mean higher game performance.
- Demographics
    - Age (In number of years): It refers to the chronological age of an individual in years at the time of data collection. This variable is considered as numerical in this study.

- Sex at birth: It refers to sex assigned at birth. Categories for this variable are male and female.
- Level of education: It refers to the highest degree or level of school completed by the participants. Categories for this variable are elementary school, high school, bachelor's degree, master's degree, and higher.
- Technology savvy: This categorical refers to the familiarity and experience of the participants with technology. It will be collected and measured based on the number of technological devices they use and the frequency of their usage.
- Living status: It refers to the participants' living condition. Categories for this variable are living alone, living with family, and living in an institution
- Cognitive status: It refers to the level of cognitive functioning. This variable includes two components: the MoCA score, ranging from 0 to 30, and the QuickMCI (Qmci) score, ranging from 0 to 100 for RQ2, investigating the correlation between game performance and cognitive status. Cognitive status is also defined as a binary variable, indicating whether the participant has MCI (1) or does not have MCI (0) for RQ4 that investigates the associated factors to MCI.

- State anxiety level: This numerical variable refers to the participant's anxiety levels when administering the traditional cognitive screenings and when playing the game. It is measured through the State-Trait Anxiety Inventory and ranging from 20-80. The higher scores correspond to the higher level of anxiety.
- System usability: This numerical variable refers to the quality attribute that indicate how easily users can utilize a technology. It is measured through System Usability Scale

(SUS), which ranges from 0-100 (152). Higher scores correspond to more usability of the technology.

3.7 Recruitment

An email containing information about the study will be sent to partner organizations, including hospitals, memory clinics, day programs, assisted living facilities, retirement homes, and community groups. Additionally, flyers will be posted in various locations within the University of Alberta Medical Clinics, at community organizations that agree to support the study, and on social media platforms. The flyers will provide details about the research opportunity and the contact information of the researcher.

If an organization shows interest, an information session will be held to provide further details about the project and address any questions from the staff and potential participants. Older adults from these partner organizations who can provide informed consent and are interested in participating can directly contact the researcher to obtain more information or express their interest in participating. Individuals who see the flyer and contact the researcher can ask questions and receive more information through email, phone calls, or in-person or online meetings.

Interested older adults who meet the inclusion criteria will provide their contact information to the researcher to schedule an introductory session and a potential data collection session. During the introductory session, potential participants will learn about G3, its functionalities, and how to use the computer to play the game. The potential participant will be also asked to read some sentences aloud to ensure they can follow the instructions, read, and understand the content. The researcher will screen participants based on the inclusion and exclusion criteria, observing for any physical or communication difficulties that could negatively impact their engagement with the game. Even if participants do not meet the inclusion criteria, they will still be allowed to play the game to maintain their dignity.

Those who meet the inclusion criteria and express interest in the study will sign a consent form provided by the researcher. The researcher will facilitate this process to ensure all participants clearly understand what their participation involves and the nature of the study. Participants will have the opportunity to play the Level 1 of the game to become familiar with the laptop and the game itself. Following consent, the researcher, in collaboration with the partner organization if applicable, will schedule the data collection session either on the same day or at a later date.

3.8 Data collection

Following the introductory part and the signing of the consent form by potential participants, demographic information will be gathered. Measurements for state anxiety will be administered before doing the cognitive test and before playing the game. The MoCA and Qmci for assessing cognitive status, will be administered following assessing the state anxiety. Participants will then have the opportunity to play G3 across six stages featuring three difficulty levels: easy, normal, and hard in a progressive order based on the items in the shopping list. The difficulty levels are determined by the number of items on the shopping list, allowing for a progressive challenge to their cognitive abilities within a controlled environment. After completing the game, the SUS will be administered. All measurements are expected to be conducted in a single data collection session, lasting approximately 120 minutes. If participants feel tired or need a break, accommodations will be made to ensure their comfort and well-being, including the option to take breaks or reschedule the session as needed. Assessments that will be used in the data collection are as follows:

- Montreal Cognitive Assessment (MoCA)

MoCA is one of the most common paper-based cognitive tests that has been discussed earlier in this proposal.

- Quick mild cognitive impairment (Qmci)

Qmci is one of the paper-based cognitive tests that has been discussed earlier in this proposal.

- State-Trait Anxiety Inventory (STAI)

The Spielberger STAI is a paper-based self-administered instrument comprising 40 items, designed to independently evaluate State Anxiety (S-Anxiety) and Trait Anxiety (T-Anxiety). S-Anxiety, assessed through 20 items, reflects a transient emotional condition influenced by the current situational context, wherein respondents indicate their immediate feelings. Conversely, T-Anxiety, also measured through 20 items, denotes a stable predisposition towards anxiety, with respondents reporting their general feelings (153). This STAI demonstrated robust psychometric properties. Test-retest reliability for the T-Anxiety subscale is high, indicating stability, whereas the S-Anxiety subscale is less stable, reflecting situational influences. Internal consistency is strong for both T-Anxiety and S-Anxiety (154). Concurrent validity is supported by strong correlations with other anxiety measures, and construct validity is evidenced by higher scores among psychiatric patients and during stressful situations (154). The total score ranges from 20 to 80, with scores of 20–39 indicating low anxiety, 40–59 indicating moderate anxiety, and 60–80 indicating high anxiety (153). In this study, the state anxiety score will be used to compare the level of anxiety experienced during the administration of traditional cognitive screening tests (i.e. MoCA and Qmci) and while playing the G3 game.

- System Usability Scale (SUS)

SUS is a paper-based, simple, subjective, 10-item scale that provides a general view of usability. Each item on this Likert scale presents a statement, and respondents indicate their degree of agreement or disagreement on a 5-point scale. The SUS is typically used after respondents have had an opportunity to use the system being evaluated, but before any discussion occurs. Respondents should provide their instant responses to each item without overthinking. The final score ranges from 0 to 100 (Ref).

3.9 Data analysis

To explore the difference between game performance in PwMCI and healthy comparison group (RQ1), the Unpaired t-test or Mann-Whitney U test as appropriate (155), with an α level of 0.05, will be applied. If the mean difference is statistically significant, it indicates that G3 can classified older adults with typical cognition and older adults with MCI based on their game performance. In addition, a two-way factorial multiple analysis of covariance (MANCOVA) (155) will be performed to compare the effects of demographics as covariates on the differences between groups.

To explore the association between the game performance and traditional cognitive tests, including MoCA and Qmci (RQ2), correlational analysis (155) between the game metrics and the scores of each traditional cognitive tests, including total score sub-scores such as memory and executive functions will be conducted. If the correlation coefficient (r) is positive closer to one, it means that the concurrent validity of G3 as an MCI screening tool is good.

To investigate the diagnostic accuracy of the game-based screening (RQ3), formulas will be used as follows:

$$\text{Sensitivity: Proportion of true positives correctly identified} = \frac{\text{TP}}{\text{TP+FN}}$$

$$\text{Specificity: Proportion of true negatives correctly identified} = \frac{\text{TN}}{\text{TN+FP}}$$

$$\text{Accuracy: Overall correctness of the testx} = \frac{\text{TP+TN}}{\text{Total Population}}$$

Where TP: True Positives, TN: True Negatives, FN: False Negatives, FP: False Positives (155). Additionally, the interpretation of the Receiver Operating Characteristic (ROC) and Area Under the Curve (AUC) will be used for examination of diagnostic accuracy (155). The ROC curve is a graphical plot that illustrates the diagnostic ability of a binary classifier system as its discrimination threshold is varied. The curve is created by plotting the True Positive Rate (TPR) against the False Positive Rate (FPR) at various threshold settings (155) .

The following steps will be used to calculate the ROC curve:

Firstly, the True Positive Rate (TPR), also known as sensitivity or recall, will be determined using the formula:

$$\mathrm{TPR} = \frac{\mathrm{TP}}{\mathrm{TP+FN}}$$

Secondly, the False Positive Rate (FPR), also known as (1 - specificity), will be determined using the formula:

$$\mathrm{FPR} = \frac{\mathrm{FP}}{\mathrm{FP+TN}}$$

Finally, the ROC curve will be calculated and plotted. TPR and FPR need to be calculated for various threshold values. Then, TPR (y-axis) against FPR (x-axis) for each threshold will be plotted. The closer the ROC curve is to the upper left corner, the higher the test's accuracy, as this position represents a sensitivity of 1 and a false positive rate of 0 (specificity of 1). An ideal ROC curve has an AUC of 1.0. An AUC of 0.5 indicates no discrimination, 0.7 to 0.8 is acceptable, 0.8 to 0.9 is excellent, and above 0.9 is considered outstanding (155,156).

To investigate if the game performance is an associated factor with cognitive status controlled by demographic variables (RQ4), logistic regression analysis (157) will be used. For all variables, categories will be combined into broader categories, when possible, to improve the power of the logistic regression model (158). Chi-Square test will be used to determine if there is a significant association between variables and cognitive status. Principal Component Analysis (PCA) will be used to reduce the number of variables in a dataset while preserving as much variability (information) as possible (159). To determines which factors to retain based on explained variance, and Eigenvalue Cut-Off of 1 will be applied. Following this, logistic regression model will be run with the included variables. The performance of the logistic regression model with be evaluated using ROC analysis and test characteristics (160).

To compare the differences between the level of anxiety while playing the game and while traditional cognitive tests in older adults with typical cognition and with MCI (RQ5), either the Paired t-test or Wilcoxon Signed-Ranks test (155) will be used as appropriate, with an α level of 0.05, to compare the anxiety level in the two conditions- while playing the games and while performing MoCA. If the mean difference is significant and lower while playing the game compared with MoCA and Qmci, it means that the G3 causes less anxiety compared to the traditional cognitive screening tools.

To explore the usability of the game-based screening (RQ6), the SUS results will be calculated and interpreted as follows:

To calculate the SUS score, the following steps will be carried out: first sum the score contributions from each item. Each item's score contribution will range from 0 to 4. For items 1,3,5,7, and 9 the score contribution is the scale position minus 1. For items 2,4,6,8 and 10, the contribution is 5 minus the scale position. Second, multiply the sum of the scores by 2.5 to obtain the overall value of SU. SUS scores have a range of 0 to 100 (152). A SUS score of 85 or higher indicates exceptional usability, while a score below 70 is considered unacceptable (161).

3.10 Ethical considerations

Several ethical considerations need to be addressed in this study: First, informed consent is essential, ensuring that participants fully understand the study's purpose and potential risks, with an emphasis on honesty and transparency. This also includes clarifying that they can withdraw their consent at any time (127). Second, the autonomy of participants must be respected, allowing them to make informed decisions about their participation freely, without any external pressure (162). Providing the participants with an introductory session to become familiar with the project and the ability to stop the process and withdraw their consent could support their autonomy and independence in this study. Third, data privacy and confidentiality measures are crucial, including secure storage and controlled access (127), that will be followed according to ethics office of the University of Alberta. Fourth, the safety of participants should always be a priority, ensuring that the benefits of the study outweigh any potential risks involved (127). Fifth, researchers should provide any needed support including emotional and informational (127). Providing this support entails researchers having a deep understanding of conditions and being equipped with flexible communication to effectively address any distress that might occur (127). All these considerations will be applied by the researcher who is experienced enough in working with older adults. Sixth, researchers should avoid mentioning participants' diagnoses to prevent causing them stress and discomfort (127). Additionally, the participants should be recruited from diverse cultures and ethnicities to ensure inclusivity and equity. However, due to the nature of the G3 game, which is limited to the English language, it is not possible to recruit participants from communities that are not proficient in English, limiting the diversity and inclusivity of this game-based screening. Additionally, the western cuisine and celebrities featured in the game might not be engaging or enjoyable for individuals from non-Western cultures. Therefore, G3 is not greatly inclusive.

3.11 Limitations

This study has some limitations. the cross-sectional design involves data collection in a single session, providing only a snapshot of the participants' game performance and cognitive status. This snapshot may be influenced by transient factors such as mood at the time of data collection and environmental factors like the time of day, location (163). Although using an average of cognitive and game performance scores might offer a more accurate representation of participants' abilities, a cross-sectional design was chosen because this is the first time the G3 is being tested as a screening tool. The validity, reliability, and diagnostic accuracy of the test have not yet been confirmed, making it unethical to require older adults, who may be vulnerable, to participate in a repeated measures design study.

Another challenge is the sample size, which needs to be larger to increase the generalizability of the results and create a more reliable regression model. However, as this is a feasibility study focusing on investigating the diagnostic accuracy and concurrent validity of the G3, the sample size is approximately 60 participants. Additionally, many older adults are reluctant to participate due to health status (164), lack of support, socioeconomic limitations (165), or fear of receiving a low score on the cognitive test, potentially causing selection bias and limiting the generalizability of the results (73). Misclassification can also occur if individuals are wrongly categorized as healthy or with MCI, reducing the reliability of the study outcomes (73).

From a technical perspective, the G3 was created in English and primarily reflects Western food culture and celebrities, which may not be engaging or accessible to a diverse population of older adults, particularly non-English speakers. Furthermore, adequate or corrected vision, hearing, and upper extremity abilities are necessary to understand the instructions and play the game, excluding older adults with impairments in these areas. Despite clear and simple game rules and instructions, the use of computer games like the G3 may not be easily accessible to older adults with very low education levels or technophobia, negatively impacting diversity, inclusion, and equity.

Finally, due to financial constraints and technical considerations, data collection will be conducted at the University of Alberta or locations provided by community partners. This limitation prevents data collection at participants' homes, negatively affecting the inclusion of older adults living in remote areas or facing commuting difficulties, and potentially reducing the ecological validity, diversity and inclusivity of the game-based screening.

3.12 Timeline

I plan to complete my research project in 2026. The ethics approval will be obtained in Fall 2024. Data collection will be conducted in 9 months and will be completed in Spring 2025. Data analysis will be completed in 4 months in Fall 2025. I plan to write the papers in six months, so they will be submitted in Summer 2026.

3.13 Budget

Thesis operating grant funding request

Item	Amount (CAD)	Rationality
Commuting to locations provided by partner organizations	200	Some partner organizations are located in areas not easily accessible by public transit.

Research materials	2000	A laptop and two mice (modified for right and left-handed users). Additionally, the cost of printing paper-based assessments.
Training	200	MoCA training course
Research travel	2000	Attendance at possible conferences such as Age-Well Annual Conference, The Canadian Gaming Summit, Serious Play Conference.
Total	4400	

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