The Effect of Aging and Cognitive Decline on Spatial and Temporal Cognition

By

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Abstract

Alzheimer's disease (AD) is one of the most challenging health conditions in our century. While there is yet no cure for this degenerative disease, the earlier it is diagnosed and treated, the more effective the treatment could be. Studies show AD-related neuro-pathological changes occur years before detectable clinical symptoms appear. Therefore, a number of computer-based cognitive tests have been designed to measure different cognitive abilities such as working memory or associative memory in older adults. However, the early effects of dementia on particular aspects of spatial and temporal cognition, such as spatial encoding/updating and explicit time perception, has not received similar attention. We hypothesized that spatial encoding/updating and explicit timing are among the early symptoms of the onset of AD and can provide reliable and accurate measures for detecting the onset of cognitive decline. Thus, we designed and conducted several Virtual Reality experiments to assess human spatial encoding, spatial updating and explicit timing in different aging groups. Two new accuracy-based measures were also introduced in this work: error score for assessing spatial orientation and signed error for assessing explicit timing. The significant correlations between the participants' performance and their age and cognitive scores supported the validity of the designed measures. The conducted experiments revealed significant differences between the performances of younger and older adults, and between high- and low-cognitive functioning participants in spatial encoding, spatial updating and explicit timing tests. These results encourage development of predictive models for differentiating between cognitively-intact and cognitively declined older adults based on their performance in the spatial and temporal tests.

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Dedication

To my father, Jalal Ranjbar Pouya
and to my wife, Shadi Kashanian

Contributions of Authors

This thesis is a "sandwich thesis" consisting of five individual manuscripts. At the time of writing (August, 2017), one of the five individual manuscripts has been published in a peer reviewed journal (Chapter 2), two manuscripts have been submitted to peer-reviewed journals (Chapter 3.2, Chapter 4.2), and two have been published in peer-reviewed conference proceedings (Chapter 3.1 and Chapter 4.1).

Mr. Ranjbar Pouya was the main contributor and first author of all the manuscripts presented in this thesis. Mr. Ranjbar Pouya's contribution to this work include developing the research questions, designing the studies, performing the data extraction, conducting the analyses, writing up all manuscripts, submitting the manuscripts and responding to reviewers' comments. Dr. Byagowi contributed to the software and hardware designs in chapters 2, 3.1 & 3.2. Dr. Kelly contributed to the conception of the studies and drafting of the articles. Dr. Moussavi contributed to the conception and design of the study, and drafting of the articles.

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List of Abbreviations

AD	Alzheimer’s Disease
DE	Directional Error
ABE	Absolute Error
CoV	Coefficient of Variation
MMSE	Mini-Mental State Examination
MCI	Mild Cognitive Impairment
MoCA	Montreal Cognitive Assessment
VR	Virtual Reality
VRN	Virtual Reality Navigation
RSE	Relative Signed Error

Chapter I. Introduction

Alzheimer's disease (AD) is one of the most challenging health conditions of the century. In 2016, approximatley 564,000 Canadians 65 years of age and older were living with cognitive impairment, including dementia, which has imposed about $10.4 billion (CDN) cost per year on our society (Alzheimer Society of Canada, 2016). To date, there is no simple and inexpensive test, such as a blood test, to be used for diagnosing AD accurately and reliably (Alzheimer’s Association, 2015). Although there is currently no cure for AD, in general the earlier the disease is diagnosed, the better outcome a treatment may have (Sperling et. al., 2011). Recent studies have shown brain changes associated with AD may even begin 20 years before the appearance of significant symptoms (Villemagne, et al., 2013;Reiman, et al., 2012;Jack, et al., 2009). Due to the lack of a gold standard method for early diagnosis of AD, various computer-based cognitive tests such as working and associative memory tasks have been developed to measure various cognitive abilities of potential patients and to aid in diagnosis. Although “disorientation in time and space” has been recognized as one of the ten warning signs of AD (Preobrazhenskaya, Mkhitaryan & Yakhno, 2006), the effects of aging and cognitive decline on spatial orientation and temporal perception have not received much attention (for a review, see Lithfous, Dufour, & Després, 2013 and Grondin, 2010).

Spatial orientation is the ability to know where one’s body or an object is in relation to the surrounding environment. It consists of complex and inter-related sets of skills including perceptual skills (e.g. optical flow perception, spatial attention, and spatial memory), general skills (e.g. planning, selection/change of a strategy) and orientation skills (e.g. mental rotation, path integration and spatial updating) (Lithfous et al., 2013). Among these skill sets, the focus of the current work is on a fundamental, but less-investigated component of spatial orientation. This component, called spatial updating, is the ability to derive or update directional information about the position of external objects or ourselves after a series of active whole-body rotations and transitions (Wolbers, Hegarty, Büchel, & Loomis, 2008). We hypothesize that impairments in spatial updating is one of the early symptoms of the onset of AD.

We also investigated the changes in temporal processing as an early symptom of AD. Time perception is the cognitive representation of time that underlies the ability to organize a chronology of events. It also underpins our perceptions of past and future, and provides a context for planning and time management. Time perception can be divided into two main components: explicit timing and implicit timing (Grondin, 2010). Explicit timing means consciously making an estimation of a discrete duration in order to compare it with a previously memorised elapsed time. Implicit timing refers to temporally-structured sensorimotor activities that can predict the onset and the duration of future events such as ball catching or playing a piano. The explicit and explicit timing mechanisms are found to be controlled by different brain regions (Coull & Nobre, 2008; Praamstra, Kourtis, Kwok, & Oostenveld, 2006). Another focus of this study is on investigating the existence of age-related and cognition-related declines in explicit timing. We hypothesize that changes explicit timing is also an early symptom of AD.

To assess human spatial and temporal processing, various types of tests, including paper-and-pen tests, desktop computer tests, and more recently, Virtual Reality (VR) experiments have been employed by researchers. Among all types, VR environments have gained more popularity in human cognition studies due to their flexibility and controllability compared to the other assessment methods (for a review see Parsons, 2016). In addition, VR presentations provide more accurate and realistic experience of complex visual scenes compared to other forms of media representations (Ausburn, Ausburn, & Kroutter, 2010). It has been shown that a VR-based navigational test can detect differences between healthy controls and depressed patients that cannot be detected by a traditional measure of spatial memory (Gould, et al., 2007).

In recent years, various VR-based experiments have been designed to assess age-related cognitive impairments in older adults (e.g. Antanova et al., 2009; Carelli et al., 2011; Liu et al., 2011; Moffat et al., 2006; Rodgers, Sindone, & Moffat, 2012) including a novel landmark-less VR Navigation (VRN) experiment designed in our lab (Byagowi & Moussavi, 2012). In this series of studies, we used the VRN experiment for assessing human spatial encoding/updating in different aging groups and the localization component of the VRN test (i.e. the rotation time of a virtual building) as a verbal estimation task to assess the explicit timing ability of participants. However, to become a standard assessment, any VR test must be scientifically shown to have certain psychometric properties (Gould, et al., 2007; McGee, et al., 2000; McGee, et al., 2004), particularly test reliability and test validity (Burles, 2014 ; Mitolo, et al., 2015; Ventura, Shute, Wright, & Zhao, 2013). In this thesis, the reliability and validity of the VRN test and its embeded explicit timing test were investigated experimentally by statistical analysis.

Test reliability (Cortina, 1993; Streiner, 2003) is the degree to which a test consistently returns the same result when repeated under similar conditions. It can usually be measured by calculating the Pearson correlation coefficient between two administrations of the same test on the same group of participants (i.e. test-retest reliability). The test-retest reliability of the VRN test was examined by comparing participants' performance over two and three time points approximately 6 months apart.

Test validity is the degree to which a psychological measure assesses the characteristics that are designed to be examined by the test (American Educational Research Association, American

Psychological Association, & National Council on Measurement in Education, 1999). There are different types of validity that can be defined for a psychometric test. In this thesis, two types of validity (convergent validity and ecological validity) were investigated.

Convergent validity refers to the degree to which a test's measure is correlated with another test's measure of the same cognitive construct when they are both administered at the same time on a same group of participants. To evaluate the convergent validity of our experiment, the Montreal Cognitive Assessment (MoCA) (Nasreddine, et al., 2005) was used. MoCA is a brief measure of global cognitive function originally developed to detect Mild Cognitive Impairment (MCI - often considered as a precursor to AD). MoCA includes a number of subtests for examining cognitive components such as visuospatial ability, executive function, attention, language, abstraction, short-term memory and awareness of present time and location. Individuals with MoCA scores less than 26 out of 30 are considered as having MCI. The MoCA test has also been found to have higher classification accuracy for the detection of cognitive decline compared to the Mini-Mental State Examination (MMSE) test (Roalfa, et al., 2013), which is another commonly used test to measure cognitive impairment. More importantly, a recent study indicates a significant correlation between a decrease in MoCA score and hippocampal volume loss (Ritter, Hawley, Banks, Miller, 2017), which is known to be affected by early neuropathological processes of Alzheimer disease (AD) (Pennanen, C. et al., 2004; Irish, Piguet, Hodges, & Hornberger, 2014). Aside from purpose of examining convergent validity, we also used the MoCA test in one of our studies (Chapter 3.2) as an exclusionary criterion for excluding cognitively-declined older adults from the healthy population under study.

Ecological validity of an experiment (Brewer, 2000) reflects the degree to which the experimental findings mirror what we can observe in real world. To support ecological validity, the methods, materials and setting of the experiment must closely approximate the real-life situation under study (Shadish, Cook, & Campbell, 2002). Ecological validity of VR environments for assessing spatial orientation has remained a controvensial issue (Renner, Velichkovsky, & Helmert, 2013; Richardson, Montello, & Hegarty, 1999; Schmelter, Jansen & Martin, 2009; Sorita, et al., 2013). In this work, the ecological validity of the localization component of the VRN test was examined by building an identical but scaled-down physical replica and the effects of encoding from these environments were compared.

To assess participant's performance in VR-based navigational tasks, many previous studies used the duration spent navigating and the distance traversed, as the main dependent variables. However, these measures might be confounded by a general decline in motor and perceptual skills with aging. The other commonly used measure in navigation research is the number of successful trials completed by a participant during navigation. Although this measure provides a rough estimation of the participants' accuracy in completing a navigation task, it cannot rule out the possible use of a trial-and-error strategy. Moreover, to avoid the effect of fatigue on participants' performance, particularly in studies investigating older adults, the number of the experimental trials is usually limited. This limitation of score range could affect the discriminating power of the measure by limiting between-group variance. To address the shortcomings of the previous assessment methods, in this research we propose a new accuracy-based measurement, called Error Score. This score is based on a weighted summation of the number of unsuccessful trials in which a participant "gives up" without completion of the task, and any other plausible directional errors when a participant is attempting to accomplish our VRN test. A detailed description of the Error Score measure and its components is provided in the data analysis section of Chapter 2.

To assess participants' performance in explicit timing tasks, most studies have used the measures of coefficient of variation (i.e. standard deviation of participant's estimations divided by the mean of their estimations) and absolute error (i.e. absolute mean difference between the test interval and estimation). However, using signed error (i.e. signed mean difference between the test interval and estimation) that shows over- and under-estimation of the test interval has not received similar attention (for a review see Pande & Pati, 2010). Therefore, most of the studies in this field only reported reduced accuracy and more variability in time estimation of older adults and Alzheimer's patients with no conclusive results regarding the sign of error (Block, Zakay, & Hancock, 1998; Rueda & Schmitter-Edgecombe, 2009). By designing new VR-based verbal estimation task (i.e. estimating the rotation time of a virtual building- Chapter 4), we propose using signed error, in addition to absolute error and coefficient of variation for capturing the differences between the performances of different age- and cognitive-function groups.

1.1 Goals and Objectives

The goal of this study is to investigate whether spatial updating and explicit timing are able to provide reliable and accurate measures for detecting the onset of cognitive decline. We use the VRN test for assessing human spatial updating in different age groups, while employing its localization component as a verbal estimation task to assess explicit timing. In addition of using the traditionally-used measures, two new accuracy-based measures are introduced in this work: error score for assessing spatial orientation and signed error for assessing explicit timing. The specific objectives of this study are:

1. To design novel VR-based time-perception tests to quantify participants' performance in explicit timing and evaluate it on human participants across the age span (Chapter 4);

2. To investigate the ecological validity of the VRN encoding test, developing code for synchronization between virtual and physical models, and collect behavioral data from both young and older adults (Chapter 3);
3. To maintain an open-source rational database of participants' trajectories logged by the VRN software, writing Structured Query Language (SQL) scripts for calculating the required performance measures and checking the consistency and integrity of the produced report (Chapter 2);
4. To examine the psychometric properties of the introduced measures including test–retest reliability, age-sensitivity (i.e. correlation with age) and convergence-validity (i.e. correlation with cognitive function) (Chapter 2 & 4);
5. To investigate the potentials of the new measures in elucidating probable differences between the performance of different age groups and also between high- and low-cognitive functioning participants (Chapter 2 & 4);
6. To compare the power of the introduced measures in predicting participants' cognitive scores in comparison to traditional measures of spatial orientation and time perception (Chapter 2 & 4).

1.2 Report Organization

This report is divided into five chapters including the current introductory chapter that introduced the key concepts, objectives, and scope of the thesis. The rest of this thesis consists of four individual manuscripts including two published papers in a peer reviewed journal (Chapter 2, Chapter 4.2), one paper submitted to a peer-reviewed journal (Chapter 3.2,), two published papers in peer-reviewed conference proceedings (Chapter 3.1 and Chapter 4.1), and finally, Chapter 5 that summarizes our findings presented in the previous chapters and suggests the future directions.

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Chapter II. Using Virtual Reality for Investigating Spatial Cognition

Introducing a new age-and-cognition-sensitive measurement for assessing spatial orientation using a landmark-less virtual reality navigational task

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Age-related impairments during spatial navigation have been widely reported in egocentric and allocentric paradigms. However, the effect of age on more specific navigational components such as the ability to drive or update directional information has not received enough attention. In this study we investigated the effect of age on spatial updating of a visual target after a series of whole-body rotations and transitions using a novel landmark-less virtual reality (VR) environment. Moreover, a significant number of previous studies focused on measures susceptible to a general decline in motor skills such as the spent time navigating, the distance traversed. The current paper proposes a new compound spatial measure to assess navigational performance, examines its reliability and compares its power with those of the measures of duration and traversed distance in predicting participants' age and cognitive groups assessed by Montreal Cognitive Assessment (MoCA) scores. Using data from 319 adults (20–83 years), our results confirm the reliability, the age sensitivity, and the cognitive validity of the designed spatial measure as well as its superiority to the measures of duration and traversed distance in predicting age and MoCA score. In addition, the results show the significant effect of age cognitive status on spatial updating.

Introduction

Age-related structural changes in the brain have been shown to affect spatial navigation in older adults (Head & Isom, 2010; Moffat, Kennedy, Rodrigue, & Raz, 2007). These changes occur in regions associated with the ability to compute precise self-to-object spatial relations (egocentric orientation) as well as object-to-object spatial relations (allocentric orientation). For instance, the lateral prefrontal cortex and hippocampus, involved with allocentric orientation (Banta Lavenex et al., 2011; Zaehle et al., 2007), are shown to significantly atrophy with increased age (Moffat, Elkins, & Resnick, 2006; Raz et al., 2004). Also, previous research has shown that the volume of striatum structures in general, and the caudate nucleus in particular, which are known to be involved in egocentric orientation (De Leonibus, Oliverio, & Mele, 2005), show significant age-related degeneration (Raz et al., 2003). These age-related structural shrinkages were found to be associated with poor performance during both egocentric (Meulenbroek, Petersson, Voermans, Weber, & Fernández, 2004; Moffat et al., 2007) and allocentric (Antanova et al., 2009; Moffat et al., 2006) navigational tasks.

Although age-related impairments during spatial navigation have been widely reported in egocentric and allocentric paradigms, the effect of age on more specific navigational components used in both paradigms, such as the ability to drive and update directional information (Aguirre & D'Esposito, 1999), has not received enough attention. During any navigational task that includes finding a target, the ability to update directional information of previously seen targets after transitional and rotational movements is of great importance. By using functional magnetic resonance imaging (fMRI) and a virtual environment task, it has been revealed that visual spatial updating of object locations relative to a moving observer relies on the construction of updated representations in the precuneus, located in the medial part of the posterior parietal cortex

(Wolbers, Hegarty, Büchel, & Loomis, 2008). The precuneus is known to be involved in visuo-spatial imagery and first-person perspective taking (Cavanna & Trimble, 2006). It has been shown that applying transcranial magnetic stimulation (TMS) on the precuneus would facilitate visuospatial mental operation without a speed/accuracy trade-off (Oshio et al., 2010). Although this cortical area has not traditionally received enough attention because of the absence of focal lesion studies, it has been shown that the volume of the right-side precuneus of individuals with parietal cortex lesions was significantly correlated with their poorer performance on a virtual maze task (Weniger, Ruhleder, Wolf, Lange, & Irle, 2009) compared to those of controls. Also, a study of MRI volumetry during virtual maze navigation (Weniger, Ruhleder, Lange, Wolf, & Irle, 2011) showed that amnestic mild cognitive impairment (MCI) individuals had significantly reduced right-side precuneus and inferior parietal cortex volumes, whereas smaller volumes of the right-side precuneus were associated with poorer performance. These findings encourage further investigation for detecting the onset of decline in spatial cognition as a predictor of brain volume reduction.

In this study, we propose using a novel virtual reality (VR) environment, previously designed by our team (Byagowi & Moussavi, 2012), to investigate the existence of age-related decline in spatial updating. Older adults have shown some impairment in landmark recognition (Kessels, van Doormaal, & Janzen, 2011), free recall of landmarks encountered along the path (Cushman, Stein, & Duffy, 2008; Monacelli, Cushman, Kavcic, & Duffy, 2003), and recall of the temporal order of the landmarks (deIpolyi, Rankin, Mucke, Miller, & Gorno-Tempini, 2007). Our designed landmark-less VR environment consisted of a three-storey cubic building with multiple identical rooms, allowing for the investigation of spatial updating capabilities beyond plausible short term memory impairments. It should be noted that we use the term “landmark-less” for our VR environment because it lacks salient objects, other than the virtual building's internal structure, that can be used by the navigator as visible reference points for finding the target room; all the walls of our VR building look exactly the same, particularly from the inside, except the front wall that has the entrance door on the first floor. According to distinctions made by Darken and Sibert (1993) between landmarks and other generic components of cognitive maps, we believe that our VR environment can be well explained without mentioning object landmarks in terms of the other cognitive map components such as districts (i.e., inside/outside of the building, floors, rooms), edges (i.e., walls and the fence), and nodes (i.e., start point, decision points on each floor and target room). However, we acknowledge that the entrance door of the building and the entrances to each floor might still be considered "landmarks" by a broader definition of this term. It is worth mentioning that our previous pilot experiment showed that making the building fully symmetric, by putting an entrance door on every wall of the building, made the encoding process too difficult for older adults due to lack of finding a unique reference object. Thus, the current paradigm was designed to maximize the reliance on updating directional information after turns, while minimizing the contribution of memory, to provide a novel approach for investigating age-related detrimental changes in spatial orientation.

Our paradigm requires a person to navigate in the VR environment to locate the position of a previously seen target; the target position can only be encoded in terms of categorical directions (e.g., left, right, back, and front) with respect to the entrance of the person into the VR building. In this paradigm, there is no training phase and no constant route to be learned, and the position of target changes randomly among the eight trials, so the task cannot be accomplished by remembering either a series of behavioural responses to familiar landmarks or a sequence of motor displacements (i.e., right or left turns). During the virtual reality navigation experiment, the participants actively walked while pushing a wheelchair, which essentially replaced the traditional use of a joystick to move through the VR environment; this not only reduces the kinetosis (motion sickness) effects but also provides vestibular and proprioceptive inputs reported to be required for accurate orientation (Féry, Magnac, & Israël, 2004; Taube, Valerio, & Yoder, 2013).

To assess people's performance in VR-based navigational tasks, many previous studies examined the time participants required to locate the target, the distance traversed, and the number of successful trials completed as the main dependent measurements (Head & Isom, 2010; Moffat et al., 2007; Moffat & Resnick, 2002). However, it is known that a general decline in motor and perceptual skills with aging can confound temporal and distance measures during navigational tasks (Lorenzo-Lopez, Amenedo, Pazo-Alvarez, & Cadaveira, 2007; Lovden, Schellenbach, Grossman-Hutter, Krüger, & Lindenberger, 2005; Taniwaki et al., 2007). Furthermore, Moffat, Zonderman, and Resnick (2001) showed that the amount of computer experience and joystick motor control had a significant effect on the time needed to complete such virtual maze learning tasks. In addition, neither completion speed nor duration of active navigation to find a target has been reported (Baumann, Chan, & Mattingley, 2012) to be correlated significantly with categorical errors, which are of interest in our study.

To address the shortcomings of the previous assessment methods, we propose a new accuracy-based measurement, called error score, which is based on a weighted summation of various plausible error types when a participant is attempting to find the target. This summation includes the number of unsuccessful trials, the number of successful trials achieved by a trial-and-error strategy, the number of errors in determining the cardinal direction of the target, the number of errors in determining the side of the building that contains the target in its correct cardinal direction, and finally the number of errors merely due to memory (i.e., which floor of the building contained the target). This comprehensive measurement is designed to capture more variability in participants' performance than the measurement of duration, distance, and each of the above-mentioned error components. To the best of our knowledge, few studies have considered a direct examination of the ability of such navigational measures to differentiate between different age and cognitive groups.

Building upon our pilot studies (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2013; Zen et al., 2013) the objectives of this study were to: (a) investigate the reliability and correlation of the proposed spatial measure with cognitive ability of participants measured by the Montreal Cognitive Assessment (MoCA) score (Nasreddine et al., 2005), and (b) investigate the ability of our proposed error score to elucidate significant differences between the performance of different age groups and also between high- and low-cognitive-function participants. We selected MoCA scores for this study as they have been found to have higher classification accuracy for detecting cognitive decline than Mini-Mental State Examination (MMSE) scores (Folstein, Folstein, & McHugh, 1975), the other commonly used cognitive-screening test (Roalfa et al., 2013). We hypothesized that our proposed error score for orientation capability would be correlated with age and cognitive status, and would be a stronger predictor than other measurements such as traversed distance and time duration needed for task completion.

Method

Participants

Three hundred and nineteen individuals (211 females) with an age range of 20 to 83 years (average age: 59.6 ± 14.2 years) and MoCA score range of 19 to 30 (average score: 27.5 ± 2.5) participated in this study (see Table 1). All participants were screened for any neurological or psychiatric disorders, and had normal or corrected-to-normal vision; they signed an informed consent form approved by the Health Research Ethics Board of the University of Manitoba prior to participation. Although a MoCA score 26 and lower is usually indicative of some mild impairment, the study participants with a low MoCA score (between 19 to 26, 78 individuals) were not diagnosed with MCI, and they were all living independently. A detailed description of the MoCA results for this group of subjects is provided in Table 2. It should be noted that 18 of these participants received one extra point in their final MoCA score for having 12 years or less of formal education as instructed by MoCA guidelines. To determine any significant differences between the obtained scores and the maximum possible scores, one-sample *t*-tests (two-tailed) were applied to each of the seven sections of the MoCA score. The results showed that the group with lower total MoCA scores (≤26) obtained significantly lower scores for all seven sections. The MoCA assessment and VRN experiment were administered by a research assistant who was not involved in data analysis.

Table II-1 Age and MoCA groups (Mean ± Standard deviations)

Age Groups	Age	MoCA	Sample Size
Younger Adults (20 -40)	28.3± 6.1	28.7 ± 1.3	38
Middle-Age Adults(41-60)	55.2± 4.2	28.0 ± 2.2	94
Older Adults(61-83)	68.6 ± 5.6	27.1 ± 2.8	177

MoCA Groups	Age	MoCA	Sample Size
Low [19-26]	65.5 ± 11.7	24.3 ± 1.8	78
Medium [27-28]	60.0 ± 13.5	27.5 ± 0.5	105
High [29-30]	56.1 ± 14.9	29.6 ± 0.5	131

Table II-2. Detailed description of the MoCA results for 78 participants with MoCA score ≤26

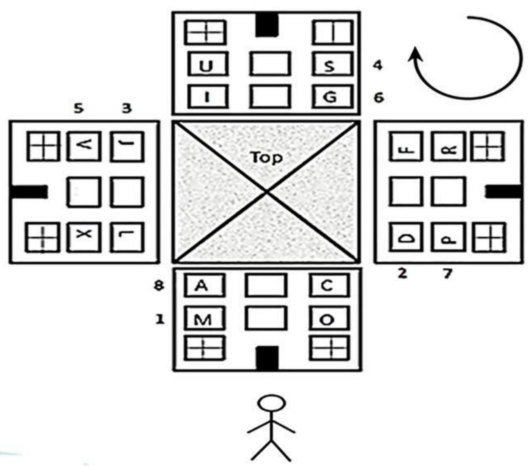
	Min	Max	Mean ± Std	Test Value	Mean Diff	t-value	Sig.
Visuospatial /Executive	2	5	4.0 ± 0.9	5	-1.0	-9.0	0.00
Naming	1	3	2.8 ± 0.4	3	-0.2	-4.1	0.00
Attention	2	6	5.3 ± 1.0	6	-0.7	-5.9	0.00
Language	1	3	2.4 ± 0.5	3	-0.5	-9.2	0.00
Abstraction	0	2	1.8 ± 0.5	2	-0.2	-4.1	0.00
Memory	0	5	2.0 ± 1.4	5	-2.9	-18.9	0.00
Orientation	2	6	5.6 ± 0.9	6	-0.4	-4.1	0.00
MoCA score	19	26	24.3 ± 1.8	27	-2.7	-12.7	0.00

To find probable differences between various age groups' performances, the population was divided into three equal-size intervals (20 years). For detecting the effect of cognitive status (measured by the MoCA score) on the performance, the participants were considered in terms of their three cognitive groups: low ($19 \le \text{MoCA} \le 26$), medium ($27 \le \text{MoCA} \le 28$), and high ($29 \le \text{MoCA} \le 30$). We used the cut-off value of 26 for defining our low-cognitive group as it is commonly used in the literature, and the high accuracy of the MoCA test for detecting MCI individuals is reported with this cut-off value (Nasreddine et al., 2005). The specifications of the groups are summarized in the Table 1.

Experiments

We used the naturalistic VRN experiment (Figure 1a), designed by our team (Byagowi & Moussavi, 2012), to assess the spatial performance of our participants. In brief, it includes navigation in a three-storey cubic building that looks identical from every side; each floor has two rooms (with windows) on each side of the building except for the entrance that is only on the front wall on the first floor. During each of the eight trials of the experiment, one of the 16 rooms on the second or third floor of the VR building is chosen as the target room by placing an "X" mark in the window of the target room, this target was only visible from outside the building (Figure 1a and 1b). Before the subject entered the building, if necessary, the building was rotated clockwise through 360 degrees (40 seconds) for the participant to see the location of target room (X in the window) from outside the building. The participant was then asked to go inside the VR building and find the target room through the mechanism of pushing a specialized wheelchair (VRNChair; Byagowi, Mohaddes, & Moussavi, 2014; Figure 2a) and navigating through the VR environment. Note that the user could either sit in the VRNChair or walk behind it; the majority of our participants preferred to walk using the VRNChair. See Appendix for details regarding the design of the wheelchair and the calibration of the optical flow according to the physical environment. The use of the VRNChair instead of joysticks to navigate in the VR environment significantly reduces the plausible kinetosis effects (Byagowi et al., 2014). The designed VR building had no internal landmarks (Figure 2b). The "X" mark in the target window was not seen unless the participant entered the correct room, in which case a recorded voice announced "Good Job" as positive feedback. This task was repeated over eight trials with different locations chosen without replacement; there were four locations, one from each side of the building, selected from each of the second and third floors. Please see Supplemental Materials containing the video files and the executable file of the program for better illustration (see Appendix C).

(a)



(b)

Figure II-1. (a) Outdoor view of the virtual building. (b) Schema of the experiment. The numbers assigned beside the walls in (b) correspond to trial numbers. On each trial (e.g., trial number 1) one of the windows beside the number (e.g., window O or M located beside number 1) would be selected randomly by the program. The selected window would be indicated with an X mark and was shown to the participants by rotating the house clockwise, if necessary. To view this figure in colour, please visit the online version of this Journal.

(a) (b)

Figure II-2. (a) Navigation in the virtual reality (VR) building was conducted by pushing the wheelchair in an open area. (b) Indoor view of one floor of the virtual building. To view this figure in colour, please visit the online version of this Journal.

For this study, after each rotation of the building and before entering the building, the participant was asked to verbally state the location of the target room. If the participant failed to correctly identify the location of the target room, the VR building was rotated for a second time. None of the participants needed to have more than two rotations to identify the orientation of the target room. In addition, at the beginning of each experimental session, every participant was given two practice trials. Every session took approximately 15–30 min to complete.

In order to investigate the reliability of the test, all participants were asked to repeat the VRN experiment after approximately 6 months had elapsed since first testing; 94 individuals and a subgroup of them (28 individuals) performed the same experiment approximately 6 and 12 months after the first experiment, respectively. The participants' MoCA scores did not change by more than 1 point between the sessions.

For assessing participants' navigation strategies, a post-test questionnaire was administered on a group of participants (66 individuals) asking for the type of strategies that they used to solve the task, if any. The participants were able to describe their navigation strategies by selecting some of the provided choices and/or writing in a free field response box. The provided choices for participants included: calculating necessary actions for reaching the target before starting movement and just following the generated actions, calculating the necessary actions during the movements, imagining themselves inside the building from a top view (survey perspective), aligning themselves with the direction of the floor entrance, and aligning with their initial direction before entering the house (egocentric perspective; note that the terms "survey perspective" and "egocentric perspectives" were not used directly in the questionnaire.

Data Analysis

During each trial of the VR navigation test, the visited room(s) along with the total distance traversed and time to locate the target was logged by the VRN software. Following our pilot studies (Ranjbar Pouya et al., 2013; Zen et al., 2013), four types of errors were calculated for measuring spatial accuracy: (a) "floor error", when the participant entered a room on an incorrect floor, (b) "side error", when the participant entered a room on the wrong side of the building but on the correct floor, (c) "left/right (L/R) error", when the participant entered a room on the correct side of the building but at the incorrect side of the wall, and (d) "totally lost", when the participant had three or more side errors during a trial, which is an indication of using a trial-and-error approach, or if the participant chose to "escape" from finishing that trial due to feeling of "being lost". During our pilot studies, a weighted sum of all errors that occurred within and over the eight trials for each participant was calculated as an overall "error score" with Equation 1 below (Byagowi et al., 2014;

Ranjbar Pouya et al., 2013; Zen et al., 2013). The reasons for selecting this particular weighting were based on the observed frequency that these different types of errors occurred in a healthy population (at the time of our pilot study), and also that the sum of the errors in a trial before being labelled as “trial-and-error” must be less than the “totally lost” error.

$$\text{Error Score} = \sum_{\text{trial}=}^{8} \text{Err}_{\text{floor}} + 4*\text{Err}_{\text{side2}} + 3*\text{Err}_{\text{side3}} + 2*\text{Err}_{L/R} + 10*\text{Err}_{\text{totally lost}} \quad (1)$$

During this study, we investigated the frequency of each of the above errors in a much larger population than that in our previous pilot studies (Ranjbar Pouya et al., 2013; Zen et al., 2013; we also investigated the correlations between error type and age or MoCA scores. Moreover, we investigated whether the total error score calculated with the above formula was representative of the overall performance error in relation to age and MoCA scores. For each participant, two independent variables (age and MoCA score) and three dependent variables, including average time, average distance, and error score (each of the detailed errors and the total error score), were analysed statistically. Average time in the VRN experiment was the average time in seconds that a participant spent attempting to find the target room during the eight trials. The average distance in the VRN experiment was the mean of the difference between the optimal desired distance and the distance traversed by the participant in the VR building in order to enter the target room during the eight trials, measured in virtual metres.

The reliability of the measurement was examined by comparing participants’ spatial performance over two and three time points approximately 6 months apart. For each session of the VRN experiment, the navigational error to reach the target location was calculated, and the Pearson correlation coefficient was calculated between the error scores. Furthermore, the age sensitivity and MoCA sensitivity of the measurement were examined by finding the probable differences between the results of three adjacent age and MoCA groups. To investigate any significant differences among the results of the different age and MoCA groups, multivariate repeated analysis of variance (MANOVA) was employed; in all instances, $p < 0.05$ was selected as the level of significance.

In order to investigate the convergent validity (Campell & Fiske, 1959), the correlation coefficients among all of the five measurements (age, MoCA score, error score, average time, and average distance) were calculated and compared. In addition, for comparing the power of error score to that of the temporal and distance variables, three multiple regression models were employed to predict, for each participant, the value of age and MoCA score based on the dependent variables as well as the value of MoCA score when age was used in addition to the dependent variables. For evaluating the significance of regression models, coefficient of determination, *R* squared (R^2), was used; this provided a measure of how well the variation in the dependent variable could be explained by the variation in the independent variable. Using the enter method, also called "forced entry", in the regression models (Cohen, Cohen, West, & Aiken, 2003), all of the independent variables (average time, average distance, and error score) were entered into the equations in one step. By inspecting the *p*-value of each predictor, we observed the relationship of predictor with target variable, while the effects of other predictors are eliminated. If one of the variables was insignificant at this stage, it showed that the variable did not contain unique information for predicting the target variable.

Results

Descriptive statistics for the participants' performance are summarized in terms of specific error types (Table 3) and general measurements of performance (Table 4). All of the variables, except floor error, passed the normality test (West, Finch, & Curran, 1995). Since the main comparisons were made by error score, which sustained the normality condition, the mentioned violation of the floor error did not affect the results.

Table II-3. Descriptive statistics of the error components.

	Floor Error	**1st F *Side Error***	**2nd F *Side Error***	**1st F *L/R Error***	**2nd *F L/R Error***	***Totally Lost***
Mean	0.1	1.2	1.1	0.5	0.4	1.8
Standard Error	0.0	0.1	0.1	0.0	0.0	0.1
Minimum	0	0	0	0	0	0
Maximum	2	7	5	4	4	8
Kurtosis	10.4	1.8	0.4	2.4	3.9	0.6
Skewness	3.3	1.3	1.0	1.4	1.7	1.1

Table II-4. Descriptive statistics for the main measurements.

	Average Time	**Average Distance**	**Error Score**
Mean ± Std	144.8 ± 56.0	26.1 ± 15.5	28.1 ± 20.2
Standard Error	3.1	0.9	1.1
Minimum	63	3	0
Maximum	400	80	80
Kurtosis	2.3	0.5	-0.8
Skewness	1.3	1.0	0.4

For better illustration of the error components, the average frequencies and their standard errors are plotted in Figure 3. The data shown support the selected weight set for constructing the measurement; the more frequent error components, which provide more within-subject variability and facilitate detecting differences, received more weights, as in Equation 1 for computing the total error score.

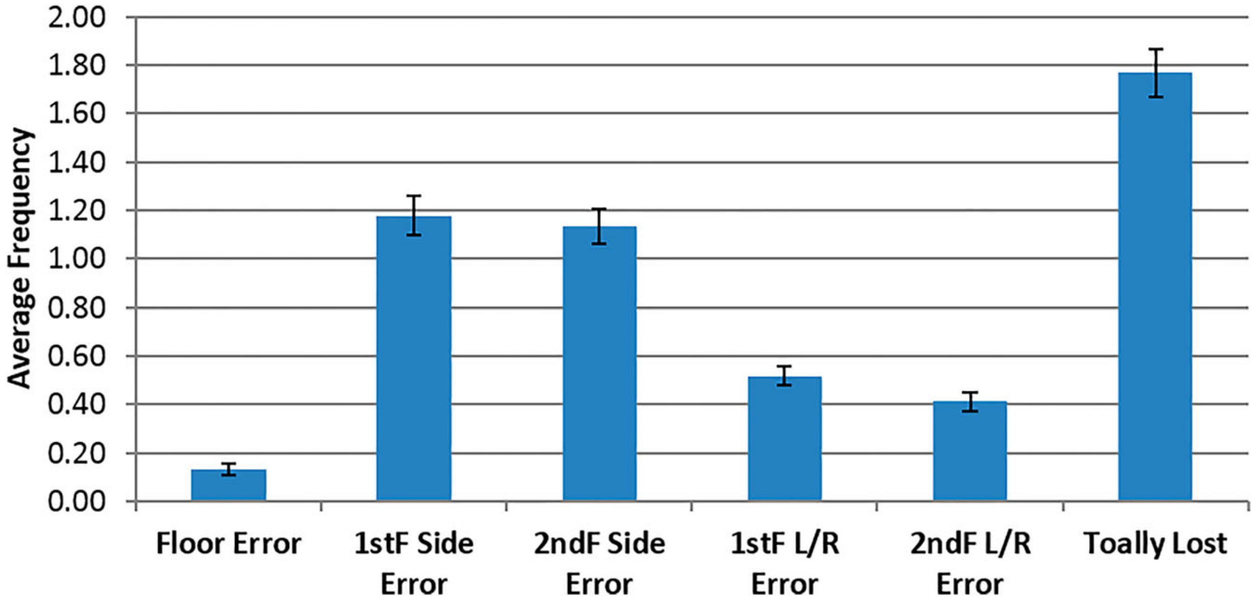


Figure II-3. Average frequencies of the error components (standard errors are reported). F = floor; L = left; R = right. To view this figure in colour, please visit the online version of this Journal**.**

It should be noted that applying MANOVA on the results revealed no significant effect of gender, $F(3, 295) = 2.08$, $p < .10$. Furthermore, no significant interaction was observed between gender and age groups, $F(6, 590) = 0.598$, $p > .05$, as well as gender and MoCA groups, $F(6, 590) = 0.598$, $p > .05$, supporting no difference between the performance of males and females in either age or MoCA groups.

Reliability of Error Score

The results of repeated tests for those who participated in two or three repeated sessions of the same VRN experiment suggest an acceptable test–retest reliability for the error score: $r = .70$

between first and second sessions ($N = 94$, $p < .001$), and $r = .76$ between the second and third sessions ($n = 28$, $p < .001$).

Age effect

The results of the dependent variables for different age groups are shown in Table 5 and Figure 4. As can be seen, there is an obvious incremental pattern for error score, average distance, and average time with age. Applying MANOVA on the results revealed a highly significant main effect for age groups for all of the dependent variables, $F(6, 590) = 7.74$, $p < .0005$. Employing Bonferroni post hoc analysis showed that all of the pairwise differences between the age groups on all of the dependent variables were significant (maximum $p < .006$). These results support the strong effect of age on the measurements.

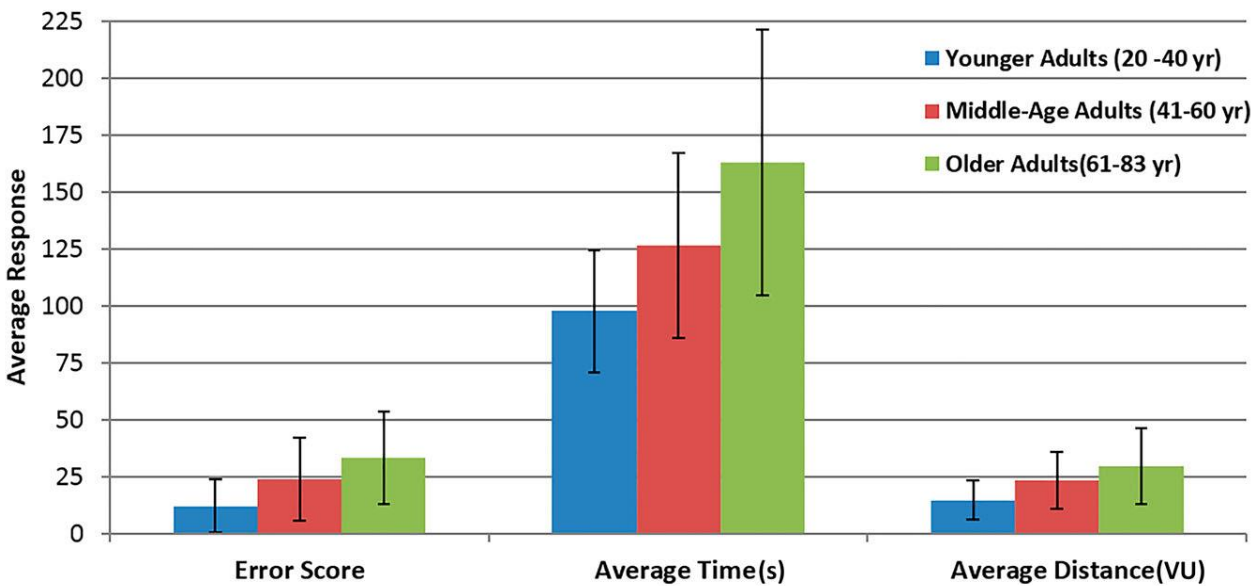


Figure II-4. Results of the three age groups on the dependent variables (bars indicate standard deviations). To view this figure in colour, please visit the online version of this Journal.

Table II-5. Results of the age groups on the three main measurements.

Age Groups (year)	Error Score	Average Time (sec)	Average Distance (m)
Younger Adults (20-40)	12.0 ± 11.8	97.7 ± 26.8	14.5 ± 8.6
Middle-Age Adults (41-60)	23.8 ± 18.3	126.4 ± 40.8	23.3 ± 12.5
Older Adults (61-83)	33.2 ± 20.2	162.8 ± 58.4	29.7 ± 16.5

MoCA effect

Table 6 shows the mean and standard deviations of the dependent variables for different MoCA groups. As can be seen, there are noticeable differences among the groups on all of the measurements in favour of cognitive performance. In other words, the higher the MoCA score, the better the spatial performance. Although the MANOVA did not show a significant main effect for MoCA groups, $F(6, 590) = 0.90$, $p < .49$, Bonferroni post hoc analysis showed that the difference between the low-MoCA group and the high-MoCA group was highly significant for all of the dependent variables ($p < .0005$ for both error score and average time, and $p < .03$ for average distance). Also, the difference between the low-MoCA group and the medium-MoCA group was significant for error score ($p < .001$) and average time ($p < .005$) but not for average distance ($p < .12$). However, the difference between medium- and high-MoCA groups was not found significant on any of the outcomes.

Table II-6. Results of the MoCA groups on the three main measurements.

MoCA Group	Error Score	Average Time (sec)	Average Distance(m)
Low [19-26]	36.9 ± 20.3	167.7 ± 59.1	30.0 ± 16.1
Medium [27-28]	26.6 ± 18.0	143.5 ± 51.3	25.5 ± 13.2
High [29-30]	24.4 ± 20.3	133.0 ± 53.8	24.5 ± 16.7

Correlation Analysis

Tables 7 and 8 show the Pearson correlation coefficients between the pairwise combinations of variables (* and ** markers show the correlation values corresponding to $p < .05$ and $p < .01$ significance levels, respectively). As can be seen in Table 7, error score had the highest correlation (and consequently highest predictability) among the error components; this shows the effectiveness of the proposed combination (Equation 1). The highest correlations in Table 8 were found between dependent variables: average time, average distance, and error score; this was expected according to their definitions. Aside from these variables, the next largest correlation coefficients were found between age and average time ($r = -.48$, $p < .005$), age and error score ($r = -.41$, $p < .005$), and age and average distance ($r = -.37$, $p < .005$).

Table II-7. Pearson correlation coefficients between the error components and age and MoCA variables.

Error component	Age	MoCA
Floor Error	-.04	.09
1st F Side Error	.18**	-.18*
2nd F Side Error	.16**	-.05
1st F L/R Error	.14*	-.11*
2nd F L/R Error	.08	.09
Totally Lost	.35**	-.26**
Error Score	.41**	-.30**

Table IIII-8. Pearson correlation coefficients between all variables.

	Age	Average Time	Average Distance	Error Score
Average Time	.48**	1		
Average Distance	.37**	.61**	1	
Error Score	.41**	.57**	.79**	1
MoCA	-.29**	-.29**	-.18**	-.30**

Regression Analysis

The three employed regression models were found to be highly significant, including the model for predicating age using the dependent variables, $F(3, 314) = 35.65$, $p < .0005$, $R^2 = .25$, the model for predicating MoCA score using the dependent variables, $F(3, 311) = 16.17$, $p < .0005$, $R^2 = .13$, and the model for predicating MoCA score using age, average time, and error score, $F(3, 311) = 15.51$, $p < .0005$, $R^2 = .13$. Employing the enter method, it was found that all of the dependent variables were significant predictors of MoCA score. However, average distance was not a significant predictor of age after controlling for the effects of other dependent variables ($\beta = -0.046$, $p < .96$), and average time was not a significant predictor of MoCA score after controlling for the effect of age ($\beta = -0.10$, $p < .11$).

Post-test strategy results

The participants' responses were categorized in three groups: egocentric strategy, allocentric strategy, and undefined strategy, according to key terms used in the responses (see Appendix B.2). For instance, the participants who did not choose "imagining yourself inside the building from a top view" among the provided options, and there was no indication in their free field responses to suggest using a survey perspective of the environment, were categorized as egocentric strategy users (17 individuals; these participants mentioned the techniques such as imagining themselves inside the building in a first person perspective, aligning themselves with their direction before entering the house and planning in advanced to take a right or left turn once on the correct floor and remembering the number of left/right turns. The allocentric group contained the participants who mentioned using a bird's eye view for finding the target inside the house, aligning themselves with the entrance of building and encoding the position of the target window in regard to the entrance of the building or entrance to each floor. The undefined strategy group included the responses with not enough information to allow the participant to be categorized into the other two groups, as well as responses that contained both sets of the key terms.

Discussion

The present results show the reliability, cognitive validity, and age sensitivity of the introduced measure, error score, for evaluating spatial orientation. This measure was based on several error components (i.e., floor error, side error, L/R error, and totally lost error), each measuring a different level of spatial orientation deficit. Note that the "totally lost" error in our designed measure provided the required basis for comparing our introduced measure with all of the previous studies that used "number of successful trials" or "number of correct responses" as a main measure. The "totally lost" error captured the number of "unsuccessful trials" and "successful trials" that were achieved by trial-and-error approach. As it was expected, this type of error held the highest correlations with participant's age and MoCA score (Table 8). Our results indicate that the other types of error (side error and L/R error) also showed significant correlations with age and MoCA score; thus incorporating these error types along with the totally lost error led to having higher correlations of the overall measure of spatial orientation with age and MoCA score. In regression analysis, although the regression models obtained a relatively low power (R^2) in predicting age and MoCA score, such R^2 values are normal for large sample sizes where high variability in the data reduces the predictability of the model.

Comparing the VRN test with available paradigms

The strategies used to locate the target in our VRN experiment was reported to be mainly either allocentric or egocentric strategies; thus, the observed age-related decline found in this study is congruent with the previous studies showing age-related impairments during spatial tasks designed for engaging allocentric (Antanova et al., 2009; Moffat et al., 2006; Rodgers, Sindone, & Moffat, 2012) and egocentric orientations (Barrash, 1994; Moffat et al., 2001; Wilkniss, Jones, Korol, Gold, & Manning, 1997). Another classification of the spatial strategies has been provided by Liu, Levy, Barton, and Iaria (2011) based on the use of landmarks (Liu et al., 2011), which includes: path integration without using landmarks; left/right orientation strategy (based on distances travelled and a sequence of body turns, ignoring landmarks available in the surrounding; heading orientation strategy (advances on the left/right strategy by incorporating landmarks in a body-referenced fashion; and cognitive mapping. Our VRN experiment is comparable with tests designed to engage left/right orientation and heading orientation (e.g., Arnold et al., 2013; Liu et al., 2011). For instance, Liu et al. (2011) reported a significant difference between the accuracy of younger (18–45 years) and older (46–67 years) adults in completing both of tasks designed to engage left/right orientation and heading orientation; this result is congruent with the age effect found in our study. These researchers also did not find a significant difference between the performances of their two younger age groups (18–30 years vs. 31–45 years; this would be expected as these age groups fall within the young age group of our study. However, the correlations between age and performance during their tasks was considerably weaker than those during our study [$r(632) = -.15$ for left/right orientation and $r(632) = -.30$ for heading orientation (Liu et al., 2011) vs. $r(319) = -.41$ in our study]. We attribute the stronger correlation observed in our study to the advantages of our experimental paradigm and our performance measures. First, previous research (Wallet, Sauzéon, Rodrigues, & N'Kaoua, 2009, 2013) has shown that active navigation in a VR environment is superior to passively watching and matching between videos extracted from a VR environment, which is the methodology used by Liu et al. (2011). Second, the main measurement in the aforementioned study was the number of correct responses, whereas in our study we used a weighted summation of spatial errors as our main measurement.

In regard to the effect of cognitive function on spatial navigation, our results are consistent with the findings that show a significant effect of cognitive level, measured by MMSE, on the performance of healthy older adults in landmark-less virtual maze task (Carelli et al., 2011). However, it should be mentioned that some route learning tasks have been reported to be insensitive to differentiating between cognitively impaired individuals and age-matched controls (Cushman et al., 2008).

Considering non-navigational paradigms, our VRN paradigm can be compared with pointing tasks (Farrell & Robertson, 1998) that are widely used to assess spatial orientation. During the pointing task, after showing a number of targets (objects) to the participant, the participant is rotated, with vision restricted, to face another direction and is asked to point to the true position of the named target from this new orientation; the location the participant points is evaluated by measuring the distance between the actual position of the target and the position indicated by the participant. It is suggested that young-to-middle age adults (average 45 years old) are able to automatically update their direction to targets, measured by accuracy and latency of target pointing, after blindfolded self-rotation to their left or right (Farrell & Robertson, 1998). However, research shows that the ability to mentally change one's perspective declines with age more so than does the ability to mentally rotate objects (Inagaki et al., 2002). Also, the performance of the elderly in a perspective-taking task was found to be inferior to that of young university students with respect to general response time and the percentage of correct responses made (Watanabe, 2011). Our results are in agreement with these findings, and this was expected as the perspective-taking task was found to be an accurate predictor of unique variance, over the mental rotation task, in navigational tasks requiring the updating of self-to-object representations (Kozhevnikov, Motes, Rasch, & Blajenkova, 2006). However, the pointing tasks do not directly examine navigation abilities and, maybe due to this limitation, were sometimes found incapable of differentiating between Alzheimer's patients and healthy older adults (Kalová, Vlček, Jarolímová, & Bureš, 2005).

Neurological implications

According to recent studies (Huang & Sereno, 2013; Lithfous, Dufour, & Després, 2013), the human mental navigation network includes retrosplenial cortex, posterior parietal, precuneus, parahippocampal, premotor, and occipital regions. As stated before, visual spatial updating of object locations relative to the moving observer was found to be dependent on the precuneus, located in the medial part of the posterior parietal cortex (Wolbers et al., 2008). Lesions to this area were shown to affect navigation performance (Weniger et al., 2009), and precuneus volume was found to be significantly reduced in MCI patients as well as correlated with poorer orientation performance (Weniger et al., 2011). The significant difference found in our study between the low-MoCA group and the rest of the participants is congruent with these findings. However, it should be noted that other areas in addition to the prenucus are involved in the process of spatial updating and are shown to be affected by MCI. For instance, it is known that both encoding and retrieval/imagery of spatial information require translation between egocentric and allocentric representations of space, mediated by posterior parietal and retrosplenial areas (Byrne, Becker, & Burgess, 2007). Both posterior parietal cortex (deIpolyi et al., 2007) and retrosplenial area (Roalfa et al., 2013; Serino & Riva, 2013) were reported to be affected by MCI and Alzheimer's disease. Aguirre and D'Esposito (1999) showed that the ability to remember and derive directional information (left and right) from a specific landmark is affected by lesions in the retrosplenial cortex. Nevertheless, Moffat et al. (2006) and Moffat (2009) reported reduced activation in retrosplenial area by normal aging that might explain the observed age effect in our study.

Limitations and future directions

One of the limitations of the current study is not having a parallel spatial evaluation such as the Questionnaire on Spatial Representation (Pazzaglia & De Beni, 2001), for comparing participants' preference for survey representation (by splitting the participants into high and low survey preference), and Perspective Taking/Spatial Orientation Test (Hegarty & Waller, 2004; these measures may have provided additional support for the validity of our proposed VRN experiment.

The obtained results suggest that high variation provided by our measure would facilitate differentiating age and cognitive groups, regardless of any employed task paradigm. Moreover, based on the properties of error score, employing this measure in a longitudinal study can provide useful information for detecting the onset of cognitive decline in older adults and perhaps be used as a warning sign for the onset of degenerative diseases such as Alzheimer's.

Appendix: The VRNChair design

The participant sits in the wheelchair, while a laptop is placed on a wooden tray, which rests on the handle bars of the wheelchair. The participant moves in the VR environment by moving the VRNChair. The VRNChair has a custom designed motion capture unit that acquires and estimates properties of the system motion with the help of two encoders (for acquiring) and a microcontroller (for estimating) the motion. The two off-axis magnetic encoders are mounted on the VRNChair's main wheels and generate relative pulses, which are transferred to the microcontroller unit. The microcontroller estimates the magnitude and the direction of the movement for both wheels by capturing the received pulses from the encoder. This estimation is based on the relationship between the velocity of each wheel and the motion of the wheelchair that has been embedded in the microcontroller as a kinematic model. The difference between the velocity magnitudes of the two wheels causes rotational velocity. In addition, the regularity of the radii of the two wheels causes translational movement. The outcome of this kinematic model is sent to the laptop as the input for movement in the VR environment with a very low latency (less than two milliseconds) using a USB 2.0 interface. The protocol used for sending the navigation input to the laptop is Human Interface Device (HID) standard, similar to a standard joystick. The “Drive Medical, Silver Sport 2–Dual Axle” wheelchair is used to design the VRNChair technology.

The optical flow of transitional movement is calibrated such that distance traversed in the physical environment is reflected by a scaled down (logarithmic) distance in the VR environment to limit the exploration space of the participant and to prevent him/her from colliding with the walls in the physical space of the experiment. However, the rotational movement is calibrated such that a rotation of 360° by the VRNChair in the physical environment produces exactly 360° of rotation in the virtual environment. In summary, the designed VRNChair merges the sense of motion observed by the vision (optical flow) with the inertial sense of motion of the participant. Our experimental observations show that our design removes motion sickness in older adults.

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Chapter III. Investigating the Ecological Validity of VR Localization on Younger and Older Adults

3.1. Investigating the Ecological Validity of VR localization on Younger Adults

The Effect of Physical and Virtual Rotations of a 3D Object on Spatial Perception

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Abstract — We question whether a virtual reality (VR) environment produces the same spatial perception as natural world. In this study, as a first attempt to answer the above question, we examined the perceived rotation of an object (a building) in both virtual and natural environments on spatial ability of 30 young males, while navigating in a virtual environment. We calculated the number of errors they made in finding a destination in a virtual reality navigational environment. The subjects performed three sets of 4 trials of finding a target room in a virtual building with no landmarks. At the beginning of each trial the target room was shown to the subject by rotation of the building from outside perspective. The building rotation was achieved in three conditions: 1) in virtual environment, 2) in real environment by rotating an identical but scaled physical building, and 3) by walking around the physical model. Each subject performed 4 trials of virtual navigation under each of the above conditions. In each trial, the traversed distance and the visited rooms were recorded by the program. One-way analysis of variance (ANOVA) was employed to find any statistical difference between the participants'' errors in three conditions. Overall, no statistically significant differences were found between the error scores in any of the three conditions. The results and their implications are discussed.

Introduction

Virtual Reality (VR) environment allows natural world emulation for different purposes by replicating real world tasks such as navigation. Experiments in a VR environment offer repeatability and flexibility to modify the testing environment. Therefore, in recent years, VR-based experiments for studying spatial perception have gained considerable attraction. The use of VR becomes more important especially when studying egocentric orientation, where the environment needs to be designed such that there are no landmarks or cues for reaching or locating the target. On the other hand, one important question arises as to whether a VR environment produces the same spatial perception as natural world.

There are some technological limitations for VR environments; they do not provide a one-to-one mapping between real and virtual perceptions. For example, the field of view is limited to the size of a monitor; thus it is narrower than the field of view available in the real world. However, studies have shown that generalization from virtual to real environments is possible (Ruddle, Payne, & Jones, 1997;Munzer & Stahl, 2008). For instance, 24 university age students learned to navigate in a VR environment with a similar accuracy to that of a real environment (Ruddle, Payne, & Jones, 1997). However, another study, examining 40 participants in the age range of 18 to 21, showed that training in VR did not provide better route learning than studying a map (Farrell, et al., 2003). These latter findings question the transfer mapping of VR to real environments or vice versa.

In this study, we investigated whether the perceived rotation of a 3-dimentional (3D) object (a building) is different in VR than in real environments. We investigated the effect of such plausible difference on the navigational performance of young adults in a VR navigational environment without any landmarks.

Method

Participants

Thirty male engineering students with an age range of 24 to 36 years (28.2±2.9) participated in this experiment. Except for two individuals, all participants were right-handed, and all had normal or corrected-to-normal vision. All participants signed an informed consent form approved by the Health Research Ethics Board of University of Manitoba prior to their participation. Known differences exist between males and females in their navigational abilities when no landmarks are provided (Moffat, Hampson, & Hatzipantelis, 1998) as well as for their mental rotation abilities (Silverman, et al., 2000). Since this was a pilot study, we recruited only adult males in order reduce the number of plausible contributing variables.

Experiments

We used a modified version of the Virtual Reality Navigational (VRN) experiment designed by our team (Byagowi & Moussavi, 2012). The modification consisted of reducing the number of trials from 8 to 4, and using an alternate error analysis. Initially we were considering the difference between shortest path to the target and the actual traversed path as the measure of error (Byagowi & Moussavi, 2012). However, such a measure of error might be biased in favor of those users experienced with VR environments. Therefore, in this study we analyzed errors such as "side error" and "Left/Right error" as described below.

The VRN environment is a virtual cubic three story building, which looks identical from each side (Fig. 1). Each side has two rooms per each floor (8 rooms on each floor) with windows towards outside. Stairs are located in the center of the building. Other than the stairs, there are no other landmarks. In this modified version of the environment, a target window was marked randomly in one of the rooms on the second floor. Each of the VRN sessions during this study had 4 trials. At the beginning of each trial, a target room's window was marked with a green color (as if the room's lights were "on"). Then, the building was rotated using a constant speed for a full circle so that the subject could see where the target room was located. After the rotation stopped, the subject was instructed to go inside the building and find the target room. The green color on the window was hidden until the subject went inside the room. After finding the target room, the system played a recorded sound of "Good Job" as a positive feedback to the participant.

The focus of this study was to investigate the difference in the perception of object rotation in VR environment, with manual rotation of the identical (but scaled down) physical object and physical rotation around the physical object in real environment. We investigated the plausible differences in perceiving either the VR or physical rotation by the accuracy of the navigation performance in the VR environment. Therefore, we repeated the 4 trials of the VRN experiment in three different settings: 1) when the VR house rotated (V), 2) when an identical (but scaled down) physical house rotated manually (M), and 3) when the subject walked around the physical house (W). In all conditions, the rotation was clockwise. The speed of rotation in "V" and "M" conditions were the same (32 sec).

The participants performed the VRN under all the above conditions. However, in order to remove the effect of any bias, we divided the participants randomly among 6 groups that performed the room finding experiment in the VR house with the following order: VMW, VWM, MVW, MWV, WVM, and WMV (to cover all possible combinations of order of rotation). Thus, each subject performed 12 trials of the VRN experiment: 4 trials for each of the conditions. Prior to the actual experiments, each subject was given two practice trials in the virtual mode. For the M and W conditions, each time, the target window was marked simultaneously both in VR and physical house; this was accomplished by Bluetooth wireless communication between the VR engine and the physical house' microprocessor. An Arduino microcontroller board inside the physical house controlled the communication of the VR and physical building to turn on the lights of the target window (with Green color) in the physical building, and also communicate with the engine to rotate it. Figure 2 shows the physical building built identically but scaled down (10:1) compared to the VR building.

Data Analysis

During our VRN experiment, the traversed trajectories of the users and the assigned target room were logged for each trial, allowing us to easily determine whether the user was navigating in the right direction or using a trial-and-error strategy to find the target room. In this study, the errors were categorized according to 3 different types: 1) "Side Error", when the subject was searching in the room on the wrong side of the building; 2) "Left/Right (L/R) Error", when the user was on the correct side of the building but chose the wrong corner of the wall; 3) "Totally Lost", when the subject tried to find the target room by trial-and-error, and 3) "Totally Lost" when three or more "Side Error" mistakes occurred.

These three types of errors were calculated separately for each participant for each of the 3 conditions of V, M, and W. To have a general error score, since the type of errors have different implications and importance, we gave a weight to each type of error, and presented the sum as the "Error Score". The given weights were 2 for "L/R Error", 4 for "Side Error", and 10 for "Totally Lost" error. The rationale for such weights was the frequency of the error among the subjects, and that the sum of the errors before categorized as "trial-and-error" must be less than the "Totally Lost" error.

The performance of each of the 6 different groups was calculated by averaging the total error (sum of the errors over the trials) of the 5 subjects in each group. The standard error of the subjects' performance in each group was also calculated. In addition, to examine whether any learning effect existed between the four trials, the error scores of all 30 subjects were averaged for each of the three V, M and W conditions, and compared between the trials. Furthermore, to investigate the relationship between the type of rotation (Virtual, Manual or Walking) and the type of error (i.e., Side Error, L/R Error, and Totally Lost) we averaged each type of error over the subjects in each condition of Virtual, Manual and Walking rotations.

Figure III-I-1 Outdoor View of the Virtual House

Results and Discussion

The mean value of the subjects' Total Error score for the 12 trials was found as 13.13±3.39 (mean ± standard error). Two outliers had error scores more than 1.5 times the interquartile range. Eleven of the 30 participants (37%) had zero errors in all of the 12 trials of the experiments. Overall, the average error of a trial was 1.16 (the ratio of mean error of the subjects to the total number of trials). The average error scores of the 6 groups (M-V-W, M-W-V, V-M-W, V-W-M, W-M-V, and W-V-R) were 3.6, 9.2, 15.2, 18.4, 14.4, and 18.0, respectively (Fig. 3).

As can be seen, the average error scores of groups are comparable to each other. As we had only 5 subjects in each group, a high standard deviation for each group's performance is expected. The high variability of the W-V-M group is due to an outlier subject with the highest error score. The difference between the first group (M_V_W) and the others seems to be large. However, it should be noted that this is not due to having knowledge transfer between the conditions, because that would necessitate reduction in the error scores as the subject proceeded across the trials; this was not the case as this group (M-V-W) had one "Side Error" in manual, one "Totally Lost" and one "R\L" errors in the virtual rotation and no errors during the walking condition.

Another important issue to address is the effect of learning on the subjects' performance. For this purpose, unsuccessful trials need to be analyzed based on the trial sequence. If significant improvements are seen during any conditions across the trials, we may conclude that participants had a reduced error score due to learning the environment. Table 1 shows the sum of each type of errors for all subjects in each of the three virtual, manual and walking rotations. As can be seen in Fig. 4 and also Table I, there is no systematic reduction in the errors from trial 1 to 4; thus, no learning effect is observed. In some conditions, the error increased in the last two trials; this could be due to fatigue or navigating to more difficult sides of the house (when the target room was on the right or back side walls , the frequency of error was observed to be higher). It is worth mentioning that each participant required approximately 30 minutes to complete the entire experiment.

It is also of interest to address is the distribution of error types for the three conditions. Figure 5 shows the average of the summed errors for each error type within each condition (virtual, manual and walking rotations). As seen in Fig. 5, the frequency of L/R error in the Walking condition is considerably less than those in Virtual and Manual conditions. The values of the other types of errors are comparable to each other whereas the Manual condition is the only one that follows a smooth transition from corner errors to totally lost errors.

As can be seen, the number of totally lost trials was the lowest for the virtual condition, whereas the walking condition had the fewest visits to an incorrect room. However, it should be mentioned that according to Fig. 4 most of the incorrect rooms visited in the Walking condition were associated with Side Errors. This compensates for the lower R/L error in Walking condition; thus, overall the Walking and Manual rotation conditions had the same total error (Table II). Finally, in order to compare the total performance across the conditions, we summarized the results in Table II; the numbers are the sum of the errors over all trials for each condition:

We also employed one-way analysis of variance (ANOVA) on the, traversed distance and the difference between the traversed distance and the minimum distance to the target room for each of the conditions. The results showed no significant differences among the conditions.

Overall, the results of the experiments presented in this paper are congruent with previous studies (Lloyd, Persaud, & Powell, 2009; Schmelter, Osmann, & Heil, 2009), suggesting no significant difference between virtual and real environments for assessing spatial abilities in young people.

In a pilot study (Lloyd, Persaud, & Powell, 2009), the real-world route learning performance was compared with that of a desktop virtual town. The results indicated similar performances in real and virtual environments, with comparable error rates and no differences for strategy preferences. Moreover, where the effect of age was investigated using younger children, older children, and adults, the results revealed equivalent age effects in real and virtual worlds (A. Schmelter, 2009). This shows that the pattern of differences concerning the performance on spatial tasks between the three age groups were comparable in the real and the virtual world conditions. However, none of the aforementioned studies investigated the performance of young adults and elderly in virtual and natural environments. Our observation in older population (unpublished recent data) is that the mapping that is required to transfer between virtual and real world settings occurs with more difficulty compared to that in young adults. Therefore, we aim to run the same experiments as in this study in older population and compare the results. To the best of our knowledge, considering the direct comparison of perception in VR and physical rotation and its effect on accuracy of navigation as investigated in this study, there has been no counterpart.

Table III-I-1 Sum of different types of errors for each condition and each Trial

		Virtual Rotation (V)	Manual Rotation (M)	Walking Around (W)
Trial 1	# of L/R Error	0	1	1
	# of side Error	4	0	1
	# of totally lost	3	3	2
	Error score	46	32	26
Trial 2	# of L/R error	1	3	1
	# of side error	3	2	1
	# of totally lost	1	2	2
	Error score	24	34	26
Trial 3	# of L/R error	2	2	0
	# of side error	1	3	4
	# of totally lost	0	2	1
	Error score	8	36	26
Trial 4	# of L/R error	2	1	0
	# of side error	3	3	2
	# of totally lost	3	2	5
	Error score	46	34	58

Table III-I-2 Overall Comparison of the Virtual, Manual and Walking Rotations

	Virtual	Manual	Walking
Number of totally lost trials	**6**	9	10

Number of incorrect visited rooms for trials that were not marked as "Totally Lost"	19	15	**10**
Error Score	**122**	136	136

Conclusion

In this study, the effect of physical and virtual rotation on human's spatial perception (young adults only) was investigated by designing three different navigational conditions, in which the target was shown by rotating the object either: in Virtual, Manual and Walking conditions. For assessing the performance of subjects, three types of error (Side Error, L/R Error, and Totally Lost) were examined, as well as a total error score (calculated based on the weighted combination of the three error types). The results showed no significant differences among the conditions. However, overall, the virtual condition showed the lowest error scores. These results confirm the validity of using virtual reality for estimating spatial memory in young adults, especially considering that about 33% of the subjects passed all of their trials without a single mistake. Also about 80% percent of the overall 360 trials were free of any type of error. The similarity between the performances of young adult participants in Virtual, Manual and Walking conditions is an interesting finding, which encourages further investigation of older participants, allowing for the examination of whether the decline in spatial cognition is manifested more in virtual or real conditions.

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3.2. Investigating the Ecological Validity of VR localization on Older Adults

Comparisons of Target Localization Abilities during Physical and Virtual Rotating Scenes by Cognitively-Intact and Cognitively Impaired Older Adults

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Abstract- Previous studies have reported that coordinate information (i.e. distance between any two objects in a specific direction) is encoded differently from Virtual Reality (VR) and physical scenes. However, the accuracy of encoding categorical information (i.e. relative positions of objects) from VR scenes has not been adequately investigated. In this study, we used a novel rotating visual scene to study the effects of aging, prior experience with VR, and dementia on the accuracy of encoding categorical information between physical and virtual environments. We recruited a cohort of 60 cognitively-healthy older adults (Experiment 1) as well as 18 older adults with mild to moderate Alzheimer disease (AD) (Experiment 2). Healthy older adults succeeded in accurately localizing the target's position from both environments, whereas individuals with AD were only able to encode the target's position from the physical environment. Our results suggest the inability to encode from a rotating VR scene might be a symptom of dementia.

Introduction

Successful navigation in virtual reality (VR) environments primarily relies on having spared visuospatial abilities, particularly spatial encoding. To develop a functional spatial representation of a VR environment, the observer has to encode objects, their locations and the spatial relations among the objects. These spatial relationships can be encoded either by categorical information (i.e. relative positions of objects such as left/right or front/behind) or coordinate information (i.e. distance between any two objects) (Jager and Postma, 2003; Ruotolo et al, 2011). Several studies have shown distinct neuronal networks are engaged with these two types of spatial encoding (Palermo et al., 2008; Trojano et al., 2002). Distances based on the coordinate system have been widely reported to be underestimated when encoded from a VR scene compared to an identical physical replica (for a review see Renner, Velichkovsky, & Helmert, 2013). However, the accuracy of encoding categorical relationships from VR scenes has not been investigated adequately; this is the focus of our study.

The ability to encode spatial relationships is usually investigated by either providing a survey (map) view of an environment to participants or allowing them to have a direct navigation experience within an environment. These two encoding methods are shown to engage different neuronal substrates (Zhang, Copara, & Ekstrom, 2012), involve different cognitive processes (Coluccia, Bosco, & Brandimont, 2007), and lead to different types of spatial knowledge (Thorndyke & Hayes-Roth, 1982). To compare the encoding of categorical information from a physical environment and its virtual replica, an aerial (survey) view of the environment is not traditionally used. This is because survey views typically do not provide sufficient differences in the visual properties of these two types of environments to provide meaningful comparisons. Therefore, previous studies have used direct navigation of the environments to compare participants' spatial encoding abilities (Richardson, Montello, & Hegarty, 1999; Schmelter, Jansen & Martin, 2009; Sorita, et al., 2013). Generally, studies using this approach have only reported inferior spatial encoding in their designed VR environments in terms of general acquired spatial knowledge. However, they have not specifically examined spatial categorical relationships.

Using a navigational paradigm to assess spatial encoding may include potential confounding factors. First, navigating within an environment usually involves higher-order cognitive processes in addition to spatial encoding, such as proficiency with the VR interface, which has been found to contribute to substantial individual differences in the ability to acquire spatial information from a VR environment (Waller, 2000; Carelli, et al., 2011). Particularly on comparing between VR and physical environments, the differences between vestibular and proprioceptive feedback in the two environments have been found as a cofounding source of difference (Ruddle, & Lessels, 2009; Moffat, 2009; Ham et. al., 2015). However, without navigation, providing a ground-level static view of a VR environment may not always be sufficient for examining the encoding of spatial relationships among objects, as some objects or structural entities may occlude others. Therefore, during this study, we used a novel method to examine the accuracy of encoding spatial categorical relationships, which allowed us to address these remaining issues. Specifically, we developed a paradigm permitting us to examine whether participants encode spatial categorical relationships among objects in a similar manner when encoding them from a rotating physical building (model sized) or a VR replica of the building.

Rotating visual scenes or objects have been widely used for investigations of object-recognition (Vuong & Tarr, 2004; Lawson, 1999) and visual change-detection (Hollingworth & Henderson, 2004; Finlay, Motes, & Kozhevnikov, 2007). However, their application for studies of spatial encoding has not received much attention (Lehmann, Vidal & Bülthoff, 2008; Wraga, Creem-

Regehr & Proffitt, 2004). The rotating scene, which changes continuously in a regular and predictable manner, presents the observer with a different view each moment in time. The visual system has been suggested to integrate these different views into a coherent 3D mental representation (i.e. scene integration) (Lehmann, Vidal & Bülthoff, 2008; Kourtzi & Shiffrar, 1999).

In our proposed paradigm, participants are asked to attend to a target window in a virtual building (a reference object) as the building is being rotated around its vertical axis in depth of the scene (passive visual exposure). This visual target is initially not visible, but enters the observer's visual field and then subsequently disappears as the building continues to rotate. The participant is required to judge the final position of the target after the 360^{o} rotation has stopped. The position of the target can only be encoded in terms of directions (e.g., left, right, back, and front) with respect to the entrance of the building(e.g. "the target is on the left side of the building"). Therefore, the paradigm we designed may provide a complementary and novel approach for investigating spatial categorical encoding from VR and physically rotating scenes. Furthermore, this approach allowed us to examine the possible effects of participant age and prior VR experience, as well as the possible differences among healthy aging individuals compared to those with dementia, on spatial encoding abilities.

Aging is recognized as one of the important influential factors on spatial abilities (for a meta-analytic review see Techentina, Voyerb, & Voyerb, 2014). However, many previous studies comparing virtual and real-world paradigms has not included the evaluation of possible effects of aging. We have only found four studies, (Kalova et al., 2005; Cushman et al., 2008; Kalia et al., 2008; Taillade, N'Kaoua, & Sauzéon, 2015) which have directly compared age-related differences of navigational processing in physical and virtual environments. Nevertheless, these studies have focused on navigational abilities without including a direct comparison of VR and physical age-related effects on spatial encoding. Interestingly, aging has shown to have more of a detrimental effect on spatial encoding during a VR navigation task in comparison to VR map reading task (aerial view) (Yamamoto & Degirolamo, 2012). Furthermore, older adult also show slower processing speeds (Meadmore, Dror, & Bucks, 2009) and reduced activation in related brain areas when making categorical relational judgments on a 2D screen (Lai, 2016). To the best our knowledge, the effect of normal aging on spatial encoding during tasks of categorical spatial encoding from 3D rotational scenes has not been yet investigated. Following our previous study on younger adults (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2013), one of the main goals of this study was to investigate spatial encoding from VR and physical rotational scenes by healthy older adults and those with cognitive decline.

During our previous study, younger adults (24-36 years) showed a similar ability to acquire categorical spatial knowledge when presented in the form of either a physical or virtual building, and they were also able to transfer information when required to navigate through the VR building (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2013). However, compared to older adults, younger adults usually have much more experience with VR through media such as gaming prior to their participation in VR studies. Considering the reported positive effect of having VR-game experience on learning from VR environments by both younger (Murias, Kwok, Castillejo, Liu, & Iaria, 2016;Geslin, Bouchard, & Richir, 2011; Smith & Du'Mont, 2009) and older adults (Carelli, et al., 2011; Anguera, et al., 2013), we were interested in examining whether VR experience would influence older adults' ability to categorically encode spatial information from our rotational scenes. Therefore, we included two groups of older adults, with and without previous VR experience.

The last factor investigated in this study is the influence of cognitive impairment on spatial encoding. Impairment in visuospatial abilities is suggested as an early symptom of Alzheimer's disease (AD) (for a review see Iachini, Iavarone, Senese, Ruotolo, & Ruggiero, 2009). In particular, categorical spatial memory function has been shown as a discriminative factor between individuals with AD and Mild Cognitive Impairment (MCI) (Kessels, et al., 2010). However, the effect of cognitive impairment on the ability to categorical encode spatial information from a 3D rotational scene task (either VR or physical) has not yet been examined. Inspired by our previous pilot study on individuals with AD (60 – 83 years), who were only able to accurately locate a target when viewing a physical, but not a VR, building (Zen, et al., 2013), we compared the performance of a cohort of individuals with mild to moderate AD during our current task, with both the VR and physical buildings. The objective of this aspect of the study was to determine whether the ability to encode a target location from our rotating VR scene is reduced in normal age-relate cognitive decline, or whether it may be a symptom of diseased aging.

General Method

Prior to starting the experiments, participants' cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) (Nasreddine, et al., 2005). MoCA is a brief measure of global cognitive function developed to detect cognitive impairments. MoCA includes seven subtests for examining cognitive components such as visuospatial ability, executive function, attention, language, abstraction, short-term memory and awareness of present time and location, with a total score of 30; normally a MoCA score of <26 is associated with some cognitive impairment. All participants signed an informed consent form approved by the Health Research Ethics Board of the University of Manitoba prior to participation.

Participants performed a Target Mapping Phase, during which they were required to encode the location of a target item. Each participant was seated on a chair facing the entrance of a three-story building, which was presented either in a VR medium (i.e. a laptop screen) or as a scaled down (1:10) physical replica of the VR version (see Fig.III.II.1a and Fig.III.II.1b). On each wall of the building, and at each floor, there were three windows, a large central window and two identical smaller windows to the left and to the right. The building looked identical from every side, except for the front side that had an entrance door located on the first floor.

(a) (b)

Figure III-II-1 : (a) Outdoor view of the virtual building. (b) Outdoor view of the physical building (scale 10:1). For both environments, the target window is shown illuminated with a green light. The target window is located on the right hand side of the second floor for illustrative purposes only (as the position was randomized during the study).

During each trial, with either the virtual or the physical condition, one of the windows of the building was randomly chosen as the target window, which was indicated by its illumination. The target window (herein referred to as *target*) was always one the 16 left/right corner windows (never a central window) on either the 2nd or 3rd floor. To show the target to the participant, the building was virtually or physically rotated clockwise through 360° (16 seconds for one full rotation), allowing participants to view the location of the target window from outside the building (Fig. 1). See Appendix A for the technical details regarding the design of both environments.

To determine if participants learned the location of the target, after each rotation the participant was asked to verbally state the location of the target. The participant was assigned 2 points if they identified the wall on which the target was located (herein referred to a *side*) or a score of 0 if incorrect. If the participant correctly identified the side location of the target, they were subsequently asked to identify the location of the target relative to the central window (left or right); correct responses were assigned an additional 1 point. Each participant experienced six trials, the target was shown from each hidden side of the building (left, right and back) twice in a pseudo-random order. The average number of points accumulated from each side was summed. Thus, the total score of a participant could range from 0 to 9.

Experiment 1

Method

A. Participants

Sixty older adults (32 women) including 30 VR-novice and 30 VR-experienced individuals with an age range of 55 to 81 years (66.0 ± 5.7 years) were recruited for this study. As the focus of the experiment was on assessing cognitively-intact older adults, three participants (2 Novice and 1 Experienced) were excluded as they scored lower than 26 on the MoCA. The participants in VR-novice and VR-experienced were matched in terms of age and MoCA score. The participants in the VR-experienced cohort (n=29, 18 women) had participated in our previous Virtual Reality Navigation (VRN) study (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2016) approximately 8 months prior to participating in the current study. The participants in the VR-novice cohort (n=28, 13 women) had not participated in any previous VR-based experiment, nor had any other VR experience (self-reported). All participants were right-handed with normal or corrected-to-normal vision and free from any neurological or psychiatric disorders.

The participants in the VR-novice and VR-experienced cohorts were further subdivided into two groups, with one group completing the physical building task (i.e. physical group and the other using the VR task (i.e. virtual group). The participants of the subgroups (approximately 15 in each subgroup) were matched for age and MoCA score. For a summary of the participant details, see Table 1.

Table III-II-1: Specifications of participants' groups (mean ± standard deviations)

VR-Novice Cohort			
Target Mapping Group	**Age**	**MoCA**	**Sample Size(female/male)**
Physical	68.1 ± 4.1	28.4 ±1.7	13 (4/9)
Virtual	67.0 ± 5.6	28.1 ± 1.6	15 (9/6)
VR-Experienced Cohort			
Target Mapping Group	**Age**	**MoCA**	**Sample Size (female/male)**
Physical	65.3 ± 7.5	28.1 ± 1.7	14 (8/6)
Virtual	65.0 ± 5.6	28.7 ± 1.3	15 (10/5)

Our previous research (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2016), using the same navigational test on a larger group of participants, revealed no significant effect of gender on spatial updating across different ages or MoCA groups. Therefore, although we attempted to maintain a similar proportion of men and women, we did not completely balance gender in each of our experimental groups.

B. Procedures

Participants completed an initial Target Mapping phase, by either viewing the position of a target in the virtual environment (group Virtual), or the scaled-down physical model of the virtual environment (group Physical). The procedure was identical to that described in General Method section.

In the case of making correct object-centered relational judgment during the Target Mapping phase, the acquired spatial knowledge was further assessed by evaluating how well the older adults could transfer this knowledge to VR navigation. During the Navigation phase, each participant was asked to virtually navigate through the building, using a VR Navigation task previously designed and evaluated by our team (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2016) in search of the observed target window seen in the Target Mapping phase. Figure 2 shows an illustration of the experimental design.

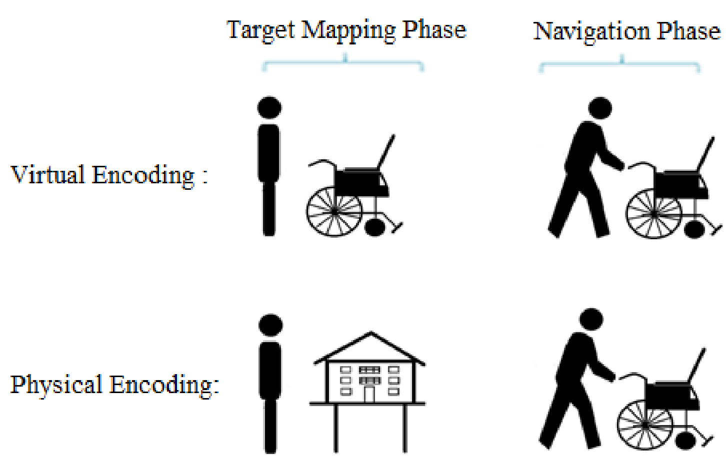

Figure III-II-2 : Schematic model of the experimental design in Experiment 1. During the Target Mapping phase, the participants observed the location of the target window in either the virtual building or the physical model building. During the Navigation phase, all participants navigated through the virtual building in search of the target window.

To move through the virtual building, participants physically pushed a specialized wheelchair (VRNChair; Fig. 3a) designed by our team (Byagowi, Mohaddes, & Moussavi, 2014). Within the virtual building, other than a set of centrally positioned stairs, there were no other landmarks (Fig. 3b). When the participant started navigating, the target window was not illuminated. However, upon entering the room with the target window, the light in the window was illuminated, and a recorded voice announced “Good Job” providing positive feedback to the participant. Once the participant successfully located the target window, a new trial was started from the same starting position in front of the building. This procedure was repeated for six trials. Before beginning the navigation phase, each participant was given two practice trials for navigation within the VR environment

(a) (b)

Figure III-II-3 : (a) Navigation in the VRN building required pushing the wheelchair through a large open room, resulting in movement within the virtual environment. (b) Indoor view of one floor within the virtual building.

C. Statistical Analyses

Target Mapping phase: As described in the General Method section (see above), participants received a score (out of a possible 9) on their accuracy in reporting the location of the target.

Navigation phase: During each trial of the Navigation phase the participants' trajectory, visited room(s) along with the total traversed distance and time to locate the target room were logged. For each participant, three dependent variables were examined: the average time (in seconds) spent navigating (navigation duration), the total traversed distance (in virtual meters) until entering the target room (navigation distance), and the "Error score" which is a weighted sum of plausible errors made by a participant when searching for the target room (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2013; Zen, et al., 2013; Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2016). This score includes the number of unsuccessful trials, in which a participant gives up without reaching the target room, the number of successful trials achieved by using a trial-and-error strategy, the number of errors in determining cardinal direction of the target (e.g., left, right, back, or front side of the building), the number of errors in determining the relative position of the target (e.g. front/back end of the left side), and the number of errors in determining the floor on which the target is located. In a recent study (RanjbarPouya, Byagowi, Kelly, & Moussavi, 2016), we have shown that Error Score is a reliable and sensitive measure when examining age-related spatial decline.

We performed a Multivariate Analysis of Variance (MANOVA) with the type of cohort (VR-Novice and VR-Experienced) and encoding condition (Physical and Virtual) as fixed factors. To test the hypotheses that experience and/or the type of environment does not affect spatial updating (a null hypothesis), a Bayesian ANOVA was employed on each dependent variable using JASP 0.8.0.0 software (JASP, 2016). The primary outcome of Bayesian ANOVA was selected as Bayes Factor (Rouder, Speckman, Sun, Morey, & Iverson, 2009) of null hypothesis over alternative hypothesis (BF_{01}).

Results & Discussion

All groups of older adults succeeded in accurately localizing the target's position from either VR or physical buildings. Therefore, there was no significant difference between encoding from virtual and physical conditions in both VR-Experienced and VR-Novice cohorts during the Target Mapping phase. For the Navigation phase, the results are summarized in terms of the average time spent navigating, the average traversed distance until the participant entered the target room, and Error score (see Table 2).

Table III-II-2: Results of the VR-Novice and VR-Experienced cohorts on the three main measurements (mean ± standard deviations)

VR-Novice Cohort			
Encoding Condition	**Error Score**	**Average Time (sec)**	**Average Distance (m)**
Physical	24.0 ± 13.5	127.1 ± 44.5	25.1 ± 16.4
Virtual	25.7± 16.5	158.0 ± 74.9	24.3 ± 14.8
VR-Experienced Cohort			
Encoding Condition	**Error Score**	**Average Time (sec)**	**Average Distance (m)**
Physical	19.9 ± 17.1	125.5 ± 42.0	22.7 ± 12.7
Virtual	22.3 ± 12.8	120.3 ± 41.4	22.1 ± 9.2

A MANOVA revealed no significant interaction between gender and the factors of interest including the type of encoding environment ($F(3, 50) = .61$, $p > 0.05$; Wilk's $\Lambda = .96$), the VR experience ($F(3, 50) = .71$, $p > 0.05$; Wilk's $\Lambda = .95$) and the encoding and experience interaction ($F(3, 50) = .51$, $p > 0.05$; Wilk's $\Lambda = .97$). The analysis also showed significant main effects for the type of encoding environment [Physical, Virtual; $F(3, 51) = .46$, $p > 0.05$; Wilk's $\Lambda = .97$], the effect of VR experience [VR-Novice, VR-Experienced; $F(3, 51) = .64$, $p > 0.05$; Wilk's $\Lambda = .96$] and no significant interaction of encoding environment and VR experience ($F(3, 51) = .83$, $p > 0.05$; Wilk's $\Lambda = .95$). Consequently, the tests of between-subjects effects revealed no significant differences for any of the dependent variables.

A Bayesian ANOVA was calculated to determine the strength of our null results. A Bayesian Factor greater than 3 is typically considered as evidence to support a null hypothesis (Rouder, Speckman, Sun, Morey, & Iverson, 2009). This ANOVA showed that for the effect of encoding environment during the Navigation phase, the null hypothesis was almost four times more likely than the alternative hypothesis on Error Score ($BF_{01} = 3.78$) and Average Duration ($BF_{01} = 3.63$), as well as about three times more likely on Average Distance ($BF_{01} = 2.88$). For the effect of experience, the null hypothesis was also shown to be more likely for the dependent variable of Average Distance ($BF_{01} = 3.25$). However, for Error Score ($BF_{01} = 2.22$) and Average Duration ($BF_{01} = 1.28$) the null hypothesis was less supported. Thus, the encoding environment provided the best support of a null hypothesis, whereas the experience was less supported. To summarize, in Experiment 1, we found no significant difference between the spatial knowledge acquired from virtual and physical rotations for both groups of VR-Experienced and VR-Novice older adults. Results from the Navigation phase revealed no significant differences between the groups.

Experiment 2

Method

A. Participants

Eighteen (8 females) volunteers with varying degrees of AD, with an age range of 57–86 years (71.4 ± 8.8 yrs) and MoCA score range of 7 to 25 (17.6 ± 6.2), participated in this study. All participants and their primary caregiver (in case a participant deemed not competent to give consent) signed the informed consent form prior to the experiments. The inclusion criteria for our study were: 1) being diagnosed of AD by their treating physician, and 2) having a MoCA score lower than 26.

B. Procedures

The procedure was identical to that described in General Method section. None of the participants with AD (n=18) were able to successfully navigate in the VR environment and being unable to find the target window. Thus, they were not assessed in navigation phase.

C. Statistical Analyses

Target Mapping phase. Statistical analyses were as described for Experiment 1, with the exception that VR experience was not considered a factor in this Experiment. Wilcoxon signed-rank test was employed to investigate any significant difference between the results of the virtual and physical rotation conditions.

Results

The AD participants, on average, obtained considerably higher scores under the physical condition (Mean ± Standard Deviation = 5.8 ± 4.3) compared to the virtual condition (1.7 ± 3.1). Wilcoxon signed-rank test showed the significance of this difference (Z= -2.87. p = 0.004).

Discussion

We proposed using a VR rotational scene as a new paradigm for the study of spatial encoding, alongside map reading and direct navigation methods. This paradigm permits the investigation into the possible differences between VR and physical categorical encoding of 3D spatial relationships. The lack of significant differences between the VR and physical encoding conditions in our previous research with younger adults (Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2013) and the current similarity found in both VR-Novice and VR-Experienced cognitively-healthy older adults, suggest the ability to encode categorical information from a rotating virtual/physical scene is affected by neither healthy aging nor inexperience with VR environments. Our results for the navigational performance of VR-Novice and VR-Experienced cognitively-intact older adults are consistent with the physical-virtual similarity in respect to aging effects reported by previous studies (Taillade, N'Kaoua, & Sauzéon, 2015; Kalova et al., 2005; Cushman et al., 2008; Kalia et al., 2008).

Our findings from individuals with AD is promising in terms of revealing a selective impairment in the processing of virtual information due to effects of dementia. This result is consistent with the previous studies suggesting the impairment in visuospatial abilities as a sign of dementia (Iachini, Iavarone, Senese, Ruotolo, & Ruggiero, 2009). Particularly, this finding may extend the reported ability of categorical spatial memory function in 2D scenes for discriminating between AD and MCI individuals (Kessels et al., 2010) to 3D scenes. In line with the results of our previous study examining individuals with dementia (60 – 83 year)(Zen et al.,2013) which showed their selective inability to encode spatial information from a rotational VR task, the results of this experiment suggest the inability to acquire categorical information from a rotational VR scene is likely a symptom of dementia.

It may be speculated that the underlying cognitive mechanism for extracting categorical information from a rotational scene is spared. However, it seems that VR rotation may not sufficiently trigger the same mechanism in AD individuals possibly due to their well-documented low-level deterioration in motion perception and depth perception by individuals with AD (Cronin-Golomb, 1995; Thiyagesh, et al., 2009). Particularly, individuals with AD are found to be impaired in their ability to construct shape-from-motion and other visuospatial production abilities (Rizzo, Anderson, Dawson, & Nawrot, 2000). However, this notion requires further investigation. Interestingly, one of our previous studies showed that individuals with MoCA scores lower than

25, and those with AD, perceive the rotational duration of the VR building differently compared to cognitively-intact older adults, as they had a significant tendency to overestimation of the rotation duration (Ranjbar Pouya, Kelly, & Moussavi, 2015). This suggests important differences in the processing of rotational motions from VR due to dementia, probably due to different low-level visual processing. Future research examining the physical mapping abilities of cognitively-intact individuals compared to those with MCI (matched for age and education along with a battery of standard neuropsychological assessments) will be necessary, and is the next steps in our program of research

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Appendix-Design of Virtual and Physical Houses

The VRN test design - The optical flow of transitional movement is calibrated such that distance traversed in the physical environment is reflected by a scaled down (logarithmic) distance in the VR environment to limit the exploration space of the participant and to prevent him/her from colliding with the walls in the physical space of the experiment. However, the rotational movement is calibrated such that a rotation of 360° by the VRNChair in the physical environment produces exactly 360° of rotation in the virtual environment. In summary, the designed VRNChair merges the sense of motion observed by the vision (optical flow) with the inertial sense of motion of the participant. Our experimental observations show that our design removes motion sickness effect well-known in virtual reality studies of older adults.

The Physical House design – The hardware used in this design was aimed to replicate the VRN building physically with a 10-fold reduction in scale (Fig. 1.b). There were 24 rooms in the building, out of which 16 could be selected randomly as target rooms. Thus, in the physical building, each room had a designated LED light on its window that was turned "ON" if the room was selected as a target. The 16 LEDs were connected using a charlieplexing configuration. Thus, only 5 pins were used to control the 16 LEDs.

The building rotated using a 12 volt battery powered, spiral-gear attached permanent magnet DC motor. In order to control the rotation and the angular velocity of the building so that it was the same for each trial, a touch-less magnetic encoder AS5134, (Austrian Micro Electronics, n.d.) was employed. The magnetic encoder provided the absolute position as well as the angular velocity.

The building was controlled using an Arduino based software running on an ATMEGA328P microcontroller. Foremost, a velocity controller loop regulated the torque implied to the actuation motor. The velocity controller was based on a proportional-differential (PD) controller. Cascading the velocity control loop, a position controller executed a trapezoidal velocity profile (acceleration, constant speed, and deceleration). This ensured a smooth rotational motion by the building to mimic the rotation in the VR. In addition, the controller of the building received commands from the host computer running the VR engine to execute appropriate commands. The commands were transmitted over a virtual serial port implemented on a Bluetooth radio link. The host computer sent a command based on the target room (window), required motion and required velocity.

Chapter IV. Using Virtual Reality for Investigating Explicit Time Perception

4.1 Using Virtual Reality to Design a Novel Verbal Estimation Task

Tendency to Overestimate the Explicit Time Interval in Relation to Aging and Cognitive Decline

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Abstract— Age-related deficits in explicit time perception has been reported by some studies. However, the findings are inconsistent about the preference of older adults to over/under-estimate the observed interval as well as the relationship between the time estimation and the participant's cognitive status. In this study, we used a verbal estimation task for the rotation time of a virtual building (40 seconds) to assess the explicit interval timing of participants. The performance of a cohort of 250 cognitively-healthy adults and 10 Alzheimer's patients was analyzed in relation to their age and cognitive scale, measured by Montreal Cognitive Assessment (MoCA) score. The participants' performances were evaluated based on three measurements: Coefficient of variation (CV) for measuring stability, Absolute Error (AE) for measuring accuracy and Directional Error (DE) for measuring the degree of over/under-estimation. A significant difference was observed between the participants who overestimated the interval and those who underestimated it in terms of age, cognitive status and Absolute Error. We also found a significant effect of time estimation, with underestimation by cognitively healthy participants to mild over-estimation by 70+ year old and low-MoCA (MoCA score < 26) participants as well as severe over-estimation by Alzheimer's disease patients. The result of regression analysis for predicting MoCA score based on the dependent variables (AE, DE and CV) support the superiority of Directional Error to Absolute Error and Coefficient of Variation that are commonly used in the time perception studies.

Introduction

Interval timing is one of the fundamental cognitive functions in daily life. Accurate estimation of an observed interval (presented by visual or auditory stimuli) requires proper functioning of various cognitive systems such as biological internal clock, attention and memory. According to Scalar Expectancy Theory (SET) theory, duration judgments are made by comparing the number of pulses counted for the observed interval in working memory with a value previously stored in short-term or long-term memory (Gibbon, Church, & Meck, 1984). Therefore, intact function of "working memory" and "episodic memory" are necessary for accurate time estimations for short and long durations, respectively. However, it is suggested that the estimation of past or future durations can give different weights to the importance of memory: estimation of an upcoming time interval with prior knowledge of its occurrence (prospective paradigm) relies primarily on attention, whereas estimation of a passed duration or event without any cue about its necessity for remembering (retrospective paradigm) basically depends on memory (Block & Zakay, 1997). Investigating the role of memory in time perception has showed that the deficits can be found selectively for durations outside the limits of working memory (beyond 30 seconds) in patients with Traumatic Brain Injury (TBI) (Schmitter-Edgecombe & Rueda, 2008;Anderson & Schmitter-Edgecombe, 2012), frontal lesions, and Korsakoff syndrome (Mimura, Kinsbourne, & O'Connor, 2000). These findings suggest the contribution of short-term episodic memory to judging intervals beyond the time frame of working memory.

Several studies have reported the tendency of older adults to overestimate the interval in prospective verbal estimation tasks (Block, Zakay, & Hancock, 1998; Rammsayer, 2001; Coelho, Ferreira, Dias, & Sampaio, 2004). Moreover, using a verbal estimation method, it was found that individuals with Alzheimer Disease overestimated time at both short (i.e., 15 s) and long (i.e., 50

s) intervals (Papagno, Allegra, & Cardaci, 2004), whereas another study on Alzheimer's reported only the overestimation in judgments of shorter intervals (5, 10 s) rather than a longer interval (25 s) (Carrasco, Guillem, & Redolat, 2000). However, most of the studies in this field relied on a prospective paradigm, and only reported reduced accuracy and more variability in time estimation of Alzheimer's patients with no conclusive results regarding the direction of error (over-estimation vs. under-estimation) (Block, Zakay, & Hancock, 1998; Rueda & Schmitter-Edgecombe, 2009). To the best of the authors' knowledge, the relationship of direction of error to age- and cognitive scale has not been investigated.

In this paper, we investigated the relationship between over-estimation of a 40-second interval and age as well as cognitive scale using a retrospective paradigm. The performance of a cohort of 250 cognitively-healthy adults and 10 Alzheimer's patients was analyzed in relation to their age and cognitive scale, measured by Montreal Cognitive Assessment (MoCA) (Nasreddine, et al., 2005) score. We hypothesize that the time interval estimation and its directional error is significantly different in aging group compared to younger adults, in participants with higher MoCA score compared to participants with lower MoCA score and also in patients with Alzheimer's compared to their age-matched healthy individuals.

Method

Participants

Two hundred fifty cognitively healthy individuals (173 females) with an age range of 20 to 83 years (60.1±14.4 yr and MoCA score of 19 to 30 (27.3±2.5) participated in this study. All of these participants had no history of neurological or psychiatric disorders. It should be mentioned that, although normally a MoCA score lower than 26 may be considered as mild cognitive impairment (MCI), none of our participants with a MoCA<26 (44 individuals) were diagnosed with MCI or Alzheimer's; they were all living and functioning independently. The specifications of the participants groups in terms of their MoCA scores are summarized in the Table 1. In addition to this cohort, 10 individuals (6 females) diagnosed with mild to moderate Alzheimer's (age: 57-86 yr, 69.4±9.0 yr; MoCA score: 7-22, 15.2±5.4) participated in this study. All participants had normal or corrected-to-normal vision; they signed an informed consent form approved by the Health Research Ethics Board of University of Manitoba prior to their participation. The MoCA assessment and the experiment were administered by a research assistant, who was not involved in data analysis.

Table IV-I-1: MoCA Groups (Means ± Standard Deviation)

MoCA Groups	Age	MoCA	Group Size
Low [19-25]	67.6 ± 9.1	23.0 ± 2.1	44
High [26-30]	58.5 ± 14.8	28.2 ± 1.3	206

Experiment

To assess the explicit interval timing of participants, we used a part of our current virtual reality (VR) experiment (Byagowi & Moussavi, 2012; Ranjbar Pouya, Byagowi, Kelly, & Moussavi, 2013), which has 8 trials of target finding by navigation in a landmark-less VR environment. In the part of experiment used in this study, a virtual cubic building is rotated clockwise through 360 degrees in 40 seconds. For the purpose of this study, participants were asked about duration of the VR building's rotation in three different trials among the 8 trials of the main experiments. No former notice was given to the participants that they would be asked about the rotation times, and no feedback was provided after their estimations; as the participants' focus in the experiment was mainly spatial performance (localizing a target in the building in 8 different trials), none of the participants answered the time interval of object's rotation by counting.

Data Analysis

After averaging the three estimations made by each participant, the following parameters were calculated for measuring temporal accuracy: 1) Coefficient of variation (CV), calculated by dividing the standard deviation to the mean of the estimations, 2) Absolute Error (AE), calculated by finding the absolute difference between the actual interval and the averaged estimation, and 3) Directional Error (DE), calculated by subtracting the actual interval from the averaged estimation (to detect over- and under-estimation of the interval). Multivariate analysis of variance (MANOVA) was employed to detect any plausible significant difference in relation to age and/or MoCA scores; in all instances $p=0.05$ was considered as the level of significance. To find age groups that significantly differ on the measurements (CV, AE and DE), a sequential search algorithm was employed to determined cut-off value along the age range. For each cut-off value, the population was divided into two age groups to find probable significant difference (p<0, 05) using MANOVA. For investigating the linear relationship between age, MoCA and the dependent variables (CV, AE and DE), Pearson correlation coefficient was calculated between the measures In addition, the regression analysis was used to predict the value of MoCA score for each subject based on the three performance measurement variable. For evaluating the significance of the regression model, R squared (R^2), was used; that provides a measure of how well the variation in the MoCA score can be explained by the variation of any of the above three performance parameters.

Results

The three performance parameters were found to be 23.1±30.1 (mean ± standard error), -11.0 ± 36.4 and 0.26 ± 0.23 for AE, DE and CV, respectively. Figure 1 shows the scatter plots of MoCA score and DE measure versus age. As can be seen in Fig.1a, there is a specific range in MoCA scores that exclusively belongs to higher age range. This range helps to find a cut-off value (herein score = 25), which distinguishes cognitively-declined older adults from healthy ones. Similarly in Fig.1b, DE measure provides almost a clear distinction between younger and older participants where no younger participants got DE above 20. Similar graphs were made for AE and CV measures versus age; however, no obvious region in the AE and CV diagrams were observed to belong exclusively to the older adults. Thus, we investigate the DE measure further.

Comparing Overestimators and Underestimators

Out of 250 participants, only 35 ones (14% of the population, 37% of male population) over-estimated ($DE>0$) the examined interval. The details of the over-estimator and under-estimators are summarized in Table II. Applying MANOVA on data of these two groups showed significant differences for age ($p<0.05$), MoCA score ($p<0.01$) and AE ($p<0.001$) but not CV ($p>0.05$).

Comparing Age groups

The only significant different between the age groups was found in comparing the participants above and below 70 years of age. Of the entire healthy participants, 157 and 55 were in 20-70 years and 70-83 years age ranges, respectively. Applying MANOVA on the results revealed a highly significant main effect of age group (for the above two age groups) using all of the dependent variables (AE, DE and CV) ($F\ (3,246) = 4.93,\ p < 0.01$). Tests of between-subjects effects revealed the significant difference between the age groups on DE ($p < 0.05$), AE ($p < 0.001$), but not on CV ($p > 0.05$). The detailed results of the age groups are provided in Table III. As it is shown, the average amount of DE shifts from -12.8 in younger adults to -0.4 in older adults; this shows a trend toward over-estimation with age. For better illustration of this trend the values of the dependent variables (AE, DE and CV) and MoCA score of the participants in the last three decades of the investigated age-range are shown in Fig.2, which clearly shows a shift from under-estimation to over-estimation by aging.

Comparing MoCA groups

The results of the MoCA groups are provided in Table IV. When the participants were grouped in terms of MoCA score of below and above 25, it was found that the Low-MoCA group over-estimated the target interval by 6.3 seconds offset and the High-MoCA group under-estimated it by 14.7 seconds offset. Using age as a co-variable in the MANOVA model, the two MoCA groups showed significant differences on AE ($p < 0.001$) and DE ($p < 0.001$) but not on CV ($p > 0.05$) measures. In Alzheimer's group, the average value of AE was found to be 110.7±165.5 (mean ± standard deviation). There was one outlier in the data (Female, 69 yrs) with AE more than two standard deviations from population mean (who overestimated the 40 seconds actual interval as 5 minutes). Five out of ten Alzheimer's participants overestimated the interval. The average DE of all them was found as +87.3 ± 180.4 including the outlier participant and +34.8 ± 74.7 excluding the outlier. After excluding the outlier, the correlation between AE and MoCA score raised to be marginally significant ($r = -0.65,\ p < 0.058$). This is equivalent to having a marginally-significant regression model for predicting MoCA score of the Alzheimer's participants based on their AE, which supports the reliability of using time perception accuracy in predicting cognitive decline.

Correlation and Regression Analysis

The correlation coefficients were found significant between age and AE ($r = 0.14, p < 0.05$), age and DE ($r = 0.15, p < 0.05$) but not between age and CV ($r = - 0.05, p > 0.05$). Also, significant correlations were found between MoCA score and AE ($r = - 0.22, p < 0.01$), DE($r = - 0.22, p < 0.01$) but not CV ($r = - 0.05, p > 0.05$). Although CV, as a measure of variation in the estimations, showed significant correlation with AE ($r = 0.24, p < 0.01$), its correlation with DE was not found significant ($r = 0.09, p > 0.05$). Using stepwise regression, the prediction model for MoCA score showed significant effect only for DE ($p < 0.001$) as the main predictor; thus, CV and AE measures were excluded from the regression model. The regression model reached significance in one step despite of having a low R squared ($F (1, 278) = 12.89, p < 0.001, R^2 = 0 .05$).

Table IV-I-2 : Grouping Based on Over- and Under-Estimation of the time interval (Mean ± Standard Deviation)

	Over-estimators	Under-estimators
Age	65.0 ± 11.1	59.4 ± 14.7
MoCA score	26.3 ±2.7	27.5 ± 2 .3
CV	0.3 ± 0.2	0.2 ± 0.3
Absolute Error	44.6 ±75.6	19.8 ± 9.6

Table IV-I-3: The Results of the Age Groups (Mean ± Standard Deviation)

	Younger Adults (20-70 yr)	Olde Adults (71-83 yr)
Age	61.9 ± 5.3	75.0 ± 3.6
MoCA score	27.3 ± 2.4	26.3 ± 2.7
CV	.25 ± .23	.29 ± .26
Absolute Error	19.4 ± 12.2	36.4 ± 59.0
Directional Error	-12.8 ± 19.0	-.4 ± 69.5

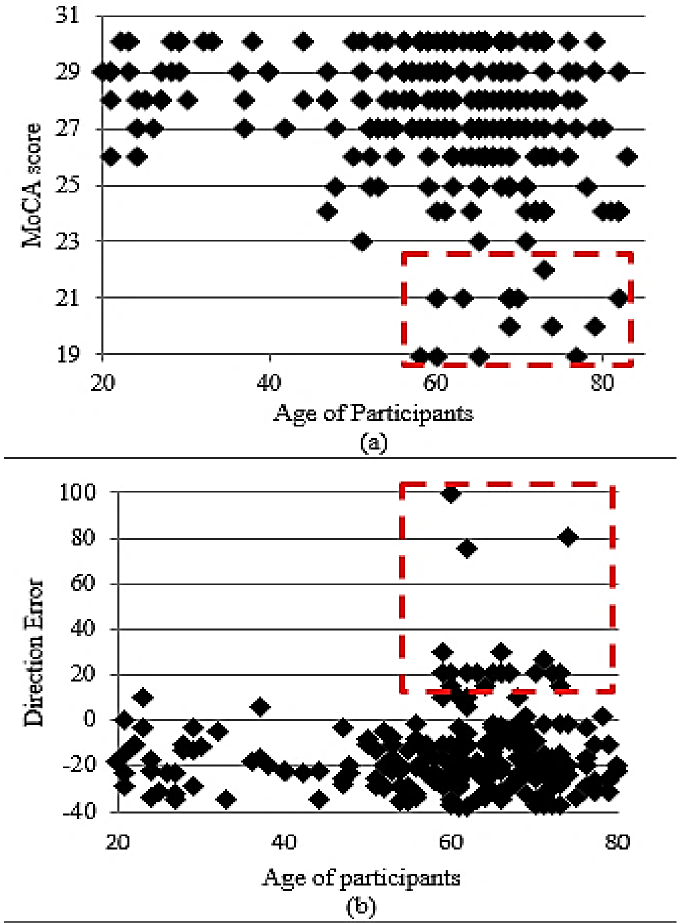

Figure IV-I-1. Comparing the distributions of MoCA score (a) and Directional Error (b) based on participants' age. The area surrounded by red rectangle indicates the scores obtained only by older adults

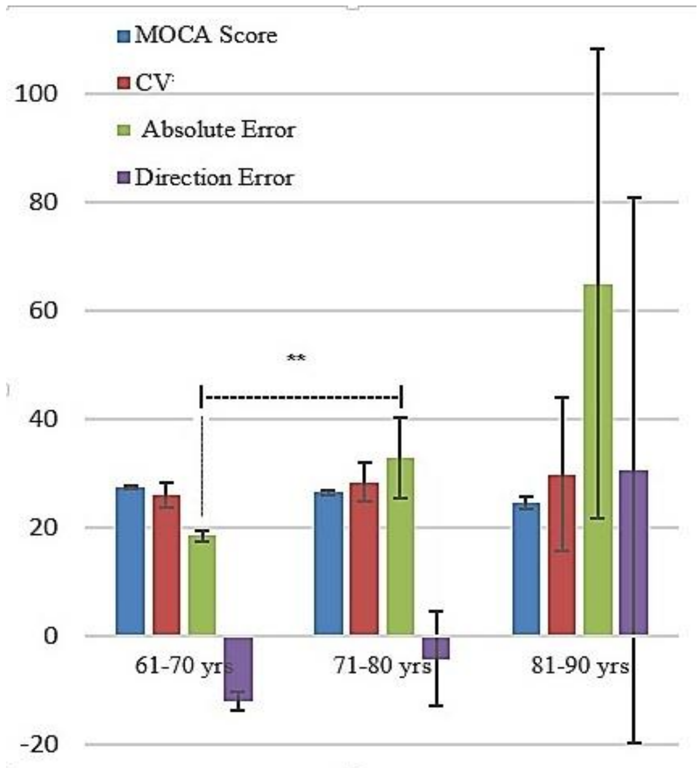

Figure IV-I-2 The value of the dependent variables (AE, DE and CV) and MoCA score of the participants in the last three decades of the investigated age-range. The Error bars show the stander Errors. The Coefficient of Variation (CV) was multiplied by 100 for illustration purpose. * indicates p<0.05 and ** indicates p<0.01

Table IV-I-4. Comparing High- and Low-MoCA Groups in the Normal Population (Mean ± Standard Deviation)

MoCA Group	CV	Absolute Error	Directional Error
High-MoCA[26-30]	0.2 ± 0.2	19.9 ± 11.6	-14.7± 17.9
Low-MoCA[19-25]	0.3 ± 0.3	38.0 ± 66.0	6.3 ± 76.1
Alzheimer Group[7-22]	0.6 ± 0.8	60.8 ± 52.7	34.7 ± 74.7

Discussion

The presented results show the validity of DE as an objective indicator of cognitive decline in normal population. Comparing participants' DEs showed that the participants, who overestimated the time interval were significantly older, and also had lower MoCA scores; their AE was also significantly higher. Although, the difference between MoCA scores of the two groups of over-estimators and lower-estimators was almost two units (25.3 vs. 27.5 for over-estimators and under-estimators, respectively), the accuracy of the over-estimators in estimating the interval, measured by AE, was almost half of that of the other group (44.6 vs. 19.8). Our results address the disparity that exists in the literature regarding the direction of error in older adults' time estimation (see (Pande & Pati, 2010) for a review). Although the hypothesis of having a slower internal clock in older adults has been supported by longer production (Perbal, Droit-Volet, Isingrini, & Pouthas, 2002; Craik & Hay, 1999), shorter reproduction (Perbal, Droit-Volet, Isingrini, & Pouthas, 2002) and subjective sensation of faster time passage (Perbal, Droit-Volet, Isingrini, & Pouthas, 2002; Fraisse, 1984), it contradicts with observing overestimation in verbal estimation task (Block, Zakay, & Hancock, 1998; Rammsayer, 2001; Coelho, Ferreira, Dias, & Sampaio, 2004).

By employing a target time beyond the framework of working memory, our results suggest that the reason of over-estimation in some groups of older adults is their difficulty in accessing temporal information from their short-term episodic memory rather than having a faster-paced internal clock. In other words, aging naturally does not lead to overestimation of the observed interval until the onset of cognitive decline. This explanation is supported by the following evidence: 1) not finding any significant differences in the performance of older adults until after seventh decade of life when their cognitive scores became significantly lower than their younger counterparts, 2) finding a considerably larger group difference in DE between the MoCA groups compared to those of the age groups, 3) higher correlation of DE with MoCA score compared to that with age, and 4) an obvious trend towards overestimation with cognitive decline: from underestimation of the interval by High-MoCA group (-14.7 ± 17.9) to mild over-estimation by low MoCA-group (6.3 ± 76.1) and severe over-estimation by Alzheimer's group ($+34.8 \pm 74.7$).

In addition, our regression analysis in normal population showed that DE is a stronger predictor of MoCA score compared to commonly used measurement of AE and CV. According to these findings, the direction of error in explicit interval timing may be considered as a potential neuropsychological assessment for detecting cognitive decline. However, one of the limitations of this study is the lack of having parallel time perception tests, such as production and re-production tasks, to compare the observed effect of overestimation. Also, recruiting a group of diagnosed MCI participants, could fill the gap between the groups of cognitively-healthy older adults and Alzheimer's patients investigated in this study. These issues are currently under investigation by our team.

Acknowledgment

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4.2 Using Virtual Reality to Design Production and Reproduction Tasks

Predicting Cognitive Status of Older Adults by using Directional Accuracy in Explicit Timing Tasks

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Abstract- The early effects of age-related cognitive decline on explicit timing have been widely reported. However, it is not clear to what extent to which measures from the internal clock and working memory are predictive of cognitive function in older adults. In this study, we examined three target intervals (i.e., 2, 6, 10 s) using Production and Reproduction tasks to assess the performance measures representative of internal clock and working memory functioning, respectively. Participants were 36 older adults (19 females) with mean age of 68.4±5.1 yr and mean Montreal Cognitive Assessment (MoCA) scores of 27.9±2.0. In the Reproduction task, the participants were asked to reproduce the duration of a previously-seen stimulus generated by a virtual reality program, whereas in the Production task the participants had to produce a target interval explicitly requested by the program. Each task consisted of nine trials with three repetitions of each target interval in a pseudo-random sequence. The average relative signed error for each target interval was calculated based on the participants' estimations. The six calculated signed errors, as well as the participant's age and gender were given as predictors for a linear regression model to determine the best predictors for the participants' MoCA scores using a backward method. The final regression model was found to be significant ($F(2, 33) = 5.06$, $p < .01$, R^2 =0.24) using only the two predictors of 6- and 10-second reproduction intervals. Our results show that measures of working memory provide a more reliable accounting of the variation of older adults' cognitive scores compared to age and the measures of internal clock.

Introduction

Time perception is the cognitive representation of time that underlies the ability to organize a chronology of events. It also underpins our perceptions of past and future, and provides a context for planning and time management. Time perception can be divided into two timing mechanisms, known to be controlled by different neural circuits: explicit timing and implicit timing (Grondin, 2010; Coull, & Nobre, 2008). Explicit timing means consciously making an estimation of a discrete duration in order to compare it with a previously memorised elapsed time. Implicit timing refers to temporally structured sensorimotor activities such as ball catching or piano practicing.

The early effects of age-related cognitive decline on explicit timing have been widely reported in literature (Grondin, 2010; Papagno, Allegra, & Cardaci, 2004; Rueda, & Schmitter-Edgecombe, 2009). However, it is not clear to what extent the reported decline in older adults' timing ability is caused by its underlying cognitive components such as internal pacemaker (i.e. internal clock) and working memory (Grondin, 2010; 2008). Furthermore, the duration of the investigated intervals in timing tasks was shown to be a critical factor due to recruitment of different brain regions in judgments of shorter and longer intervals (Penney, Gibbon, & Meck, 2008).

Previously Ranjbar Pouya and colleagues (Ranjbar Pouya, Kelly, & Moussavi, 2015) used a verbal estimation task to assess the explicit timing ability for a duration beyond the size of working memory (i.e. 40 seconds). The findings showed significant effects of aging and cognitive status on timing ability as well as a significant correlation between the signed error of estimation and cognitive score of the participants. The participants' cognitive score was assessed by Montreal Cognitive Assessment (MoCA) (Nasreddine et. al. ,2005), which is a widely-used measure of global cognitive function originally developed to detect Mild Cognitive Impairment (MCI). The assessment includes a number of subtests for examining cognitive components such as visuospatial ability, executive function, attention, language, abstraction, short-term memory and awareness of present time and location. MoCA score has also been found to have higher classification accuracy for the detection of cognitive decline compared to the Mini Mental State Examination test (Roalfa et. al., 2013) another commonly used test to measure cognitive impairment. More importantly, a recent study indicates a significant correlation between MoCA score and hippocampal volume (Ritter, Hawley, Banks, Miller, 2017), which is known to be affected by early neuropathological processes of Alzheimer disease (AD) (Pennanen, C. et al., 2004; Irish, Piguet, Hodges, & Hornberger, 2014).

Despite significant correlations, only less than 5% of the MoCA score variation could be explained by the variation of the error in the verbal estimation task (Ranjbar Pouya, Kelly, & Moussavi, 2015). This might be due to the “quantization problem” of the verbal estimation method used, which rounds the participants’ responses (Wearden, 2015). Moreover, the cognitive processes involved in the verbal estimation task could be related to both the speed of the internal clock and the performance of working memory; however, the contributions of these components to the observed variation in MoCA score were not further clarified.

To address these shortcomings, in the current study we used two non-verbal paradigms for assessing the underlying cognitive components in explicit timing of older adults: Interval Production which is involved more with the speed of internal clock and Interval Reproduction which is involved more with the performance of working memory (Baudouin, Vanneste, Isingrini, & Pouthas, 2006; Grondin, 2010; 2008). We examined three target intervals within the capacity of working memory (i.e., 2, 6, 10 s) for each of the above-mentioned paradigms. These short intervals were also selected to minimize the confounding factors such as desire to terminate the experiment sooner because of impatience or inability to delay a response.

For developing these paradigms, we used Virtual Reality (VR) technology to provide a more ecologically valid (Brewer & Crano, 2000) approach for investigating time perception tasks in which the setting of the experiment approximates real-life (Shadish, Cook, & Campbell, 2002). To the best of our knowledge, this would be the first application of VR stimulus for Interval Production and Interval Reproduction tasks. We examined the validity of the tasks we designed by attempting to replicate the classic results in this area. For instance, it is known that given the same set of target intervals, the participants' performance during production and reproduction tasks should be significantly different (Baudouin et. al., 2006;Grondin, 2010; 2008). Moreover, in each task, the participants' performance should be significantly different on estimating the intervals less than 3s compared to the longer intervals (Lewis & Miall, 2002; Coslett, Shenton, Dyer & Wiener, 2009). After examining the validity of the designed tasks, we investigated the hypothesis that using these detailed paradigms with a range of short target intervals would lead to more predictability of variations in the cognitive score.

Method

Participants

Thirty six older adults (19 females) with an age range of 61 to 87 years (μ =68.4 ± 5.1 yr) and MoCA range of 23 to 30 (μ = 27.9 ± 2.0) were recruited for this study. There were no significant differences in terms of the participants' ages and MoCA scores between males and females. Informed consent was obtained from all individual participants included in the study.

Experiments

To assess the cognitive processes involved in explicit timing, two virtual reality (VR) based version of Interval Production and Interval Reproduction tasks were designed using C++.NET

(Microsoft Visual Studio 2010) and OpenGL environments. The program consists of a user-interface, a keyboard-handler control system and an output module which records participants performance in an excel file. For handling the graphic components of the program OpenGL, Glut (OpenGL Utility Toolkit) and GLUI (GLUT-based User Interface) were used.

In the Reproduction task, the participants view a VR room. By pressing the Enter key on the keyboard, a random object appears at the center of the room (Fig. 1). The object stays in the room for an interval of time (e.g. 2, 6 or 10 sec) and then disappears. After disappearance of the object, the participants are expected to give their non-verbal estimation of the object's duration, without counting the interval, by using the following method: pressing the Space button for initiating the interval, waiting for a duration of time equal to the object's duration in the room, and then pressing Space button again to signal the end of the interval. This response method, key-pressing to start and stop the reproduction, showed higher accuracy compare to methods requiring participants to continuously press a key during the interval (Mioni, Stablum, McClintock & Grondin, 2014). The color and shape of the objects were selected randomly by the program but the appearance interval was selected using a pseudo-random sequence.

At the start of the experiment, in addition to asking participants not to count for interval estimation, they were instructed to immediately state the color and shape of the appeared object out loud. This verbal procedure was used to interfere with the possibility of using a counting strategy (i.e. distraction task). This distraction task was adopted from simplified versions of verbal repetition of random digits (Rakitin, Stern, Malapani, 2005). The random digit repetition has been shown to cause lower accuracy and higher variability during reproduction tasks (Mioni et. al., 2014), and was not found to be superior to articulatory suppression and not-to-count instructions (Rattat & Droit-Volet, 2012).

In the Production task, a set of instructions were present on the wall, which asked participants to generate an interval of 2, 6, or 10 seconds by pressing the Space button, waiting for the requested duration of time (without counting) and pressing the Space button again. The participants were instructed to press the button for the second time as soon as they felt the requested time interval "was finished".

Each task consisted of 9 trials with 3 repetitions of each target interval in a pseudo-random sequence such that two identical intervals were not consecutive and no apparent ascending/descending trend was presented in trial sequences (e.g. 2-6-10 or 10-6-2). At the beginning of each experimental session, every participant was given two practice trials for each paradigm. No feedback was given to the participants during the experiment.

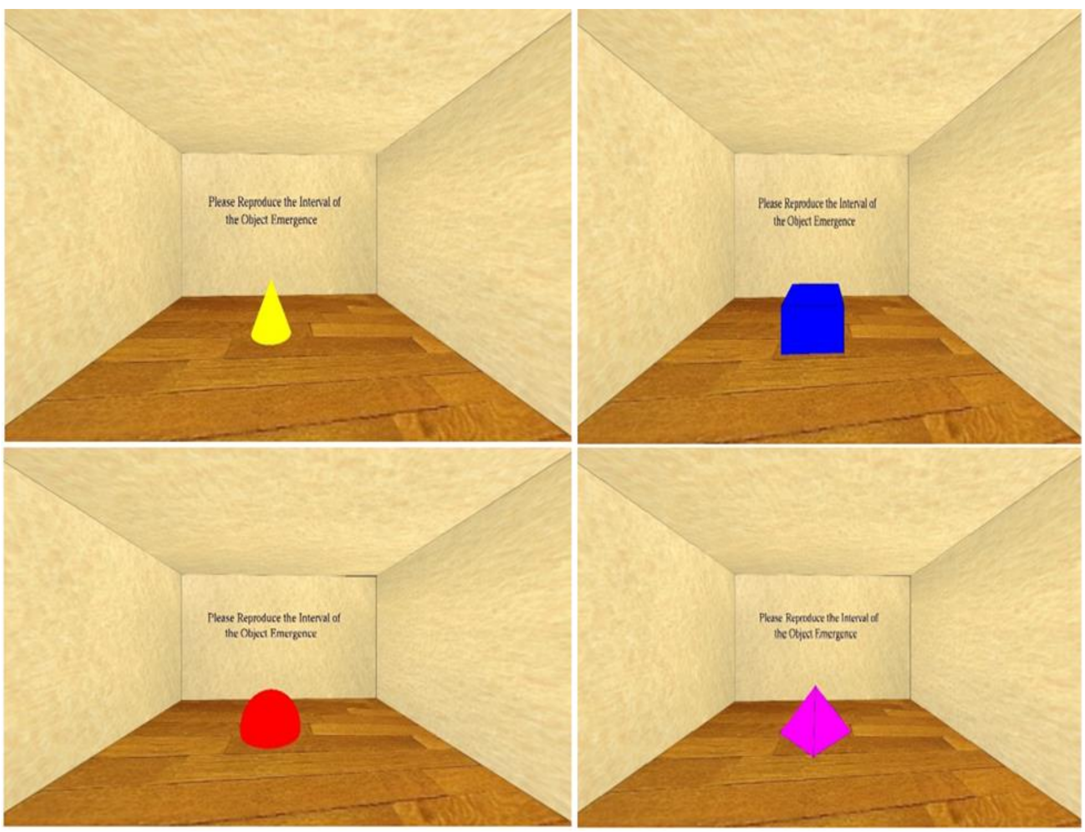

Figure IV-II-1 View of the Interval Reproduction task

Data Analysis

To assess participants' performance during explicit timing tasks, most studies have used the measures of coefficient of variation (i.e. standard deviation of participant's estimations divided by the mean of their estimations) and absolute error (i.e. absolute mean difference between the test interval and estimation). However, using signed error (i.e. signed mean difference between the test interval and estimation) that shows over- and under-estimation of the test interval has received marginal attention (for a review see Pande & Pati, 2010). Considering the reported superiority of signed error over absolute error and coefficient of variations in predicting MoCA score (Ranjbar Pouya, Kelly & Moussavi, 2015), we used the signed error as our main measurement. For both tasks, the difference in time between two button presses was recorded by the program as the participants' estimation of the observed or requested interval. The performance of the participants were then averaged for each target interval and the Relative Signed Error (RSE) was calculated as follows:

$$RSE_t^p = \frac{\left(Ave.\left(Est\ _t^p\right) - t\right)}{t} \tag{1}$$

where p indicates the paradigm of the test (i.e. Production, Reproduction) and t indicates the target interval (i.e. 2, 6 and 10 s). For showing the validity of the designed tasks, the results were analyzed using a mixed-design ANOVA with Task Type (i.e. Production, Reproduction) and Interval Duration (i.e. 2 , 6 , 10 sec) as within-subjects factors and Gender as a between-subject factor. Level of significance was selected as <.05.

The six calculated signed errors (3 for Production and 3 for Re-production task), as well as the participant's age and gender were given as predictors for a linear regression model to determine the best predictors for the participants' MoCA scores using backward method (probability of F-to-remove >= 0.1). Before applying the final regression model, the required assumptions for multiple regression were checked including lack of outliers, lack of collinearity of data, independence of errors, normality of error distribution, and homogeneity of variance of data.

Results

Descriptive statistics for the participants' performance are summarized in Table is IV-II-1. It can be seen that none of the signed errors violates the normality criteria based on the skewness and kurtosis values. Calculating Pearson correlation coefficients between the signed errors, age and MoCA score shows that only reproduction of 10-second holds significant correlations with age and MoCA score. The correlation between Age and MoCA score was also found significant (r = -.334, $p < .05$)

Mauchly's test indicated that the assumption of sphericity had been violated (χ^2 *(2) = 36.0, p < .001*), therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = 0.60$). Analysis of variance revealed a significant main effect for Task Type ($F(1,34)=8.65$, $p = .006$) and Interval Duration ($F(1.20,40.86)=13.36$, $p < .001$) as well as a significant interaction between Task Type and Interval Duration ($F(1.42,48.24)=8.52$, $p = .002$). However, there was no significant interaction between Gender and Task Type ($F(1,34)=.27$, $p = .60$) or Gender and Interval Duration ($F(1.20,40.86)=1.26$, $p = .28$). Post-hoc analysis using paired samples t-tests (corrected for multiple comparison using Bonferroni method) was applied to unfold the significant interaction between task type and target durations. None of the differences between the signed errors of 6- and 10-s durations was found significant in the both tasks. Also, the signed error for the production of 2-s was initially found significance different from the signed errors for the production of of 6- and 10-s durations but it significance did not sustain after Bonferroni correction. However, the signed error for the reproduction of 2-s duration was significantly different from those of the reproduction of 6- and 10-s durations even after Bonferroni correction.

Before applying regression analysis, an analysis of the standard residuals was carried out, which showed that the data contained no outliers (std. residual min = -2.31, std. residual max = 1.45). The histogram of the standardized residuals indicated that the data contained approximately normally distributed errors, as did the normal P-P plot of standardized residuals, which showed the data points closely lied on the diagonal line.

Table IV-II-1 : Descriptive statistics for the participants' performance.
RSE stands for Relative Signed Error. Corr. stands for correlation. * denotes significance under $p<.05$

Predictor	**Median ± Std.**	**[Min., Max.]**	**Skewness**	**Kurtosis**	**Corr. Age**	**Corr. MoCA**
$\boldsymbol{RSE^{Pro.}_{2\,sec}}$	.04 ± .30	[-0.68 ,0.72]	.08	.34	.32	.03
$\boldsymbol{RSE^{Pro.}_{6\,sec}}$	-.04 ± .24	[-.60 , .57]	.25	.76	.04	.14
$\boldsymbol{RSE^{Pro.}_{10\,sec}}$	-.04 ± .26	[-0.64 , 0.56]	.04	-.04	.00	.21
$\boldsymbol{RSE^{RePro.}_{2\,sec}}$	-.01 ± .39	[-0.73 , 1.08]	.47	.38	.05	-.02
$\boldsymbol{RSE^{RePro.}_{6\,sec}}$	-.25 ± .23	[-0.63 ,0.46]	.74	1.59	-.10	.01
$\boldsymbol{RSE^{RePro.}_{10\,sec}}$	-.24 ± .15	[-0.62, 0.16]	-.11	.64	-.35*	.40*

Testing the assumption of collinearity indicated that none of the predictors held a Variance Inflammation Factor (VIF) greater than 10 or a Tolerance factor less than 0.1 except for Production error during the 6-s duration and Production error during the 10-s duration due to having a high Correlation Coefficient (CC) among them (*CC = 0.95, p < 0.00*). Since Production error during the 6-s duration showed an additionally high correlation with Production error during the 2-s duration (*CC = 0.75, p < 0.00*), this predictor was excluded from further analysis. After removing the Production error during the 6-s duration all of the predictors held acceptable VIF Tolerance values and Multicollinearity was not a concern anymore. The scatterplot of the standardized residuals showed that the data met the assumptions of homogeneity and linearity of variance.

The final regression model was found to be significant (F(2, 33) = 5.06, p < .01, R^2= 0.24) using only two predictors of 6- and 10-s reproduction errors. The age factor was excluded in a pre-final step of the model selection. The analysis showed that the Production error during the 6-s duration did not significantly, but marginally, predict the value of the MoCA score (Beta = -0.34, t(33) = -1.82, p < .08). However, the Production error during the 10-s duration significantly predicted the value of the MoCA score (Beta = 0.60, t(33) = 3.18, p < .003). Fig. IV-II-2 illustrates the relationship between the predictors and MoCA score.

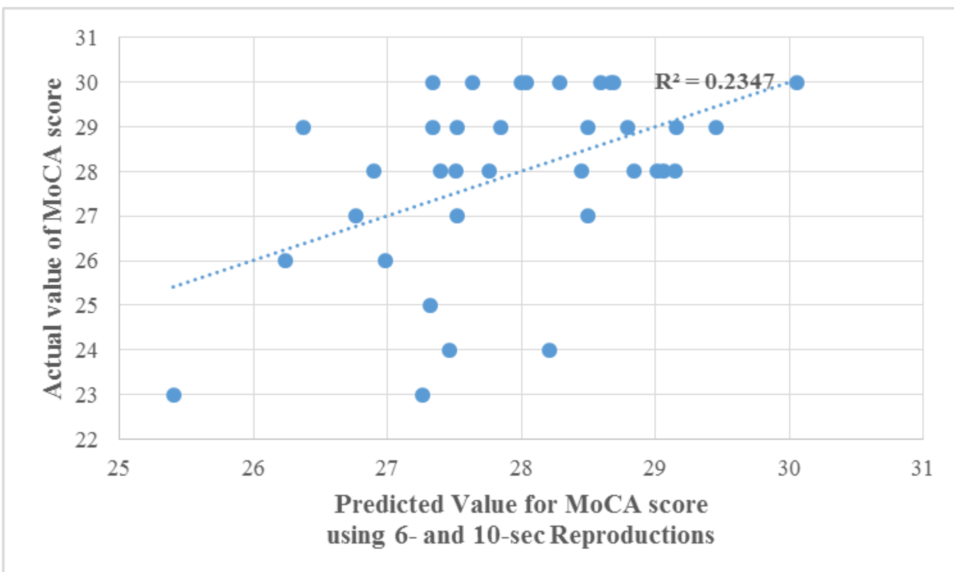

Figure IV-II-2 Scatter plot of MoCA score over 6- and 10-sec Reproduction Errors

Conclusion

In this study, we employed VR for designing standard time estimation paradigms in order to take the first step for developing a more ecologically valid time perception task. Our statistical analysis showed that our VR test could replicate the classical difference between Production and

Reproduction task, as well as the difference between timing the intervals below and above 2 seconds. The lack of sex differences in our results is also in agreement with a previous meta-analytic review (Block, Hancock, & Zakay, 2000) which showed no overall effect of sex in the prospective paradigm of interval timing (i.e. participants knew in advance they would be required to judge duration) particularly on reproduction task (Rammsayer & Rammstedt 2000). Moreover, comparing the effect of sex on different measures of timing showed there were no sex differences when the measure of relative error was used (Glicksohn & Hadad, 2011).

Considering the direction of the errors, the older adults on average under-reproduced the 6 and 10-second intervals by 20 percent, which is consistent with the reported under-reproduction in older adults in previous studies (0Perbal, Droit-Volet, Isingrini, Pouthas, 2002; Block, Zakay, & Hancock, 1998; Carrasco, Bernal & Redolat, 2001). Our findings reveal that only the signed errors of 6- and 10-second during the reproduction task explain a significant amount of the variance of the cognitive scores of older adults. This result during the time reproduction task is of importance as most of the studies on the effect of cognitive decline of time perception have used verbal time estimation tasks, whereas few studies have used time reproduction (Haj & Kapogiannis, 2016).

To the best of our knowledge, very few studies in the field of time perception to date have examined the prediction of global cognitive function measures by timing measures. Using a temporal recency task, no correlation has been found between the performance during the task and measures of frontal lobe function such as word recognition, set shifting and immediate verbal recall (Becker, Wess, Hunkin & Parkin,1993). Using verbal estimation task, significant correlations have been found in individuals with Alzheimer's disease (AD), but not in the healthy controls, between time estimations, clock-drawing scores (Barabassy, Beinhoff, & Riepe, 2007) and digit span assessment (Papagno, Allegra, & Cardaci, 2004). However, using measures of absolute errors, coefficient of variation and estimation-to-target ratio for verbal estimation test has shown almost no significant correlations between time estimation variables and neuropsychological measures for young adults, older adults and individuals with MCI (Rueda, & Schmitter-Edgecombe, 2009). Assessing individuals with AD using a temporal bisection task has not shown a significant correlation between any of the performance measures and neuropsychological tests/scales for dementia (including MMSE) (Caselli, Iaboli, & Nichelli, 2009). Previous research using a temporal production task with 3 and 10 seconds on a combined group of younger and healthy older adults showed no linear correlation with Rey auditory-verbal learning test and Raven’s Standard Progressive Matrices (Lalonde, 2010). Compared to the previous correlational study using MOCA scores (Ranjbar Pouya, Kelly & Moussavi, 2015), our method could increase the MoCA score predictability about 5 times (from .05 to .24) by addressing the quantization problem and using a range of short target intervals within the size of working memory.

Our findings suggest the measures of working memory (i.e. reproduction task errors) might be able to provide a more reliable accounting of the variation of older adults’ cognitive scores compared to age and the measures of internal clock (i.e. production task errors). It is known that the proper function of working memory depends on the prefrontal and parietal cortices (Lewis & Miall, 2003). Moreover, it has been shown that the right dorsolateral prefrontal cortex is essential in time reproduction (Jones, Rosenkranz, Rothwell, & Jahanshhi, 2004). Therefore, our results showing a connection between measures of working memory and the cognitive decline of older adults may be related to reported dementia-related atrophies of the prefrontal and parietal cortices (Trompa, Dufoura, Lithfousa, Pebayleb, & Després, 2015). Moreover, the exclusion of 2-second interval in the final model is in agreement with previous studies suggesting the primary role of the caudate and the putamen, not affected by dementia, in timing intervals below 3 seconds (Lewis &

Miall, 2002). The next step of our research is to conduct the same set of experiments on the individuals diagnosed with MCI and AD to distill out the effect of pathological aging on the investigated cognitive components.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Chapter V. Conclusions

5.1. Summary of Findings

In this series of studies, we investigated different spatial and temporal test procedures for examining the effect of age and cognitive decline on participants' performance. In the VRN test, designed to measure spatial updating performance, we showed the test has an acceptable test–retest reliability based on our newly-introduced measure of Error Score. Also, we found there was no main effect of gender, nor any interaction of gender with age and cognitive function in the VRN test. Most importantly, significant differences were found between the performances of young, middle-age and older adults, and also between high- and low-cognitive functioning participants. We showed that Error Score had significant correlations with age and cognitive function that were higher than that of the duration, traversed distance and Error Score's sub-components. Moreover, our results indicate that Error Score's power in predicting participants' age and cognitive scores is stronger than duration and traversed distance measures.

Regarding the spatial encoding test, we used a novel method, a rotating visual scene, to examine the accuracy of encoding spatial categorical relationships in both physical and virtual environments. This method of spatial encoding is innovative and quite different from common spatial encoding methods used in VR studies. Using our rotating-scene method, we investigated the possible effects of participant age and prior VR experience and dementia on spatial encoding abilities. We showed the ecological validity of the spatial updating test in younger and healthy older adults. Our results, for the first time, revealed that the inability to encode a target location from a rotating VR scene could be a symptom of dementia.

Regarding the Explicit timing test, we tested three paradigms. In verbal estimation paradigm, for a target interval beyond the size of working memory (i.e. 40 sec) participants 70-83 years old estimated the interval significantly less accurate compared to the participants 20-70 years older . In addition, performances of high- and low-cognitive functioning participants as well as AD patients were found significantly different. Consistent with our hypothesis about the effectiveness of signed error as an accuracy measure, we found significant differences between the over-estimator and under-estimators, in terms of their age, cognitive functioning and absolute error of the estimations. The correlations of age and cognitive function with the measures of explicit time perception (particularly for Signed Error) were found significant. In addition, the Signed Error's power in predicting participants' cognitive function was found superior to measures of absolute error and coefficient of variation after controlling for the effects of other measures and age. In the Production and Reproduction paradigms (Chapter 4.2) the participants estimated the intervals inside the size of working memory (i.e. 6 and 10 sec). The Signed Error of estimations showed a highly stronger correlation between explicit timing and older adults' cognitive function compared to that of the verbal estimation paradigm.

The results in this thesis are promising in terms of finding the significant correlations between the VR-based spatial and temporal tests' results and age and MoCA scores. These findings encourage developing predictive models for classifying participants into their correct cognitive groups (measured by MoCA or an alternative neuropsychological assessment) based on their performance in the spatial and temporal test. Taking this step is valuable as most of the previous studies in the field have focused only on showing statistically significant differences between the pre-defined groups of older vs. younger or cognitively-intact vs. cognitively-impaired adults.

5.2. Recommendations for Future Work

a) Recommendations for the VR Spatial Navigation test:

The significant differences found in the VR spatial assessment among cognitively-declined and cognitively-intact older adults encourages the extension of this cross-sectional research to a longitudinal approach. Considering that almost 10 years of cognitive decline (Amieva et al.,2005) and hippocampial volume loss (Fox et al.,1996; 1998) in AD preceding dementia, it is of interest to see how changes in spatial performance of older adults over time can predict conversion to AD. Particularly, performing longitudinal research has been mentioned as the first and most obvious need in the field of aging and spatial navigation (Moffat, 2009).

A longitudinal study can be designed by recruiting two age- and gender-matched groups of cognitively-declined and cognitively-intact older adults with a sample size of at least 50 participants on each group for holding acceptable test power. The VRN test can be repeated four times with at least six months interval between the assessments. Beside the VRN and MoCA tests, the following assessments is suggested to be conducted on each session (prior to the VRN test) to control for the large individual differences observed in the VRN experiment and other navigational studies:

- A questionnaire for quantifying prior experience with computers, computer-games and VR (see Appendix B.2)
- Santa Barbara Sense-of-Direction Scale (Hegarty et. al., 2002) which is a self-report measure of environmental spatial ability shown to be correlated with objective measures of performance in a number of environmental spatial cognition tasks.

- Perspective Taking/Spatial Orientation Test (Hegarty et. al.,2004) which is a is a psychometric test of spatial orientation, in which people are shown a two-dimensional array of objects, imagine taking a perspective within the array, and indicate the direction to a target object from this perspective. This test is the closest standard paper-and-pen test to the VRN test based on the conducted literature reviews.

After collecting data, the correlations between the VRN test and the above mentioned measures should be inspected. The effect of individual differences can be minimized by regression out these measures from VRN Error Score. Next, meaningful Error score changes over time can be established through defining Reliable Change Indices (RCI) (Heaton et. al., 2001; Jacobson & Truax, 1991) for each of the groups. This index can be corrected for the practice effect (Parsons et. al., 2009) might be observed across the sessions. By comparing the change index between the groups, the validity of the VRN test as a cognitive screen tool can be established.

b) Recommendations for the Virtual-Physical spatial encoding test:

Adding standard depth perception and motion perception tests to the assessment of AD patients is necessary for explaining the observed disagreement between virtual-physical encoding. A very informative approach can also be taken by examining eye movements in AD patients and controls (sex- and age-matched) during encoding the target from virtual and physical rotations. The probable differences between the groups and cross the conditions on the location, latency and duration of gaze fixation during encoding will shed more light to the behaviour findings reported in this thesis.

c) Recommendations for Time perception tests:

According to the findings in this thesis, it is recommend that the focus of future studies would be on supra-second intervals (ranges from 5-20 sec) in order to detect cognitive decline in older adults. The Interval Reproduction task showed its superiority to the verbal estimation and the interval production tasks in predicting MoCA score of older adults. In the next step, it would be of interest to compare the performance of older adults on Reproduction paradigm with that of Comparison paradigm, in which the relative duration of presented intervals should be judged. The Two common implementation of the Comparison paradigm are Temporal Generalization task and Temporal Bisection task. In Temporal Generalization task (Wearden, Denovan, & Haworth, 1997), a standard interval is initially presented several times, and participants should indicate whether subsequent intervals are of the same length as the standard. In Temporal Bisection task (Kopec, & Brody, 2010), the shortest and the longest intervals of a series of intervals are first presented several times. and are then followed by intervals, including the standards, that have to be categorized as being closer to one of the two anchored standards. Developing appropriate and valid VR programs for these tasks along with the developed programs for verbal estimation, Interval Production and Interval Reproduction may lead to the establishment of the first comprehensive VR-based Time perception battery in the field.

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Appendix A. Participant Information & Consent Form

Title of Study: "Investigating Human's spatiotemporal Perception using haptic computer games**"**

Protocol number: "___6____"

Principal Investigator: "Dr. Zahra Moussavi, Electrical & Computer Engineering, University of Manitoba

Co-Investigator: Dr. Debbie Kelly, Psychology Department, University of Manitoba

Sponsor: *"NSERC"*

You are being asked to participate in a Clinical Trial (a human research study). Please take your time to review this consent form and discuss any questions you may have with the study staff. You may take your time to make your decision about participating in this clinical trial and you may discuss it with your regular doctor, friends and family before you make your decision. This consent form may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand. This study is financially supported by the University of Manitoba and NSERC.

Purpose of Study

The objective is to test the sense of time/speed and orientation using interactive computer games. A total of 400 participants will participate in this study. The results of this study help in better understanding of human brain development and cognitive learning and also to detect the early signs of Alzheimer disease.

Study procedures

If you take part in this study, you will be instructed to play two virtual reality games. They are designed to assess human brain temporal and spatial processing abilities. You are not required to know any computer knowledge to play the games; they are fun and engaging. The games are to navigate inside a virtual building to reach a predefined destination. Once you have played the games, if interested, you may ask us to describe the data analysis procedure. To play the orientation game, you will be asked to wear a goggle and sit either in a manual wheelchair or swivel chair controller, which you will navigate it through a virtual building. Once you wear the goggle you will be totally immersed in the virtual environment and feel yourself present in that environment. The experimenter will walk beside you (in case of using the wheelchair) or stand beside you (in case of using the swivel chair) for the entire duration of the experiment to ensure you do not hit any obstacle in the real environment.

You may also take one or two cognitive tests to assess your short-term memory. There is no other requirement. If you are 50+ year old, we would encourage you to participate in our study for a few more times, each 6 months apart.

If at any time while playing the games, you decide to stop participating in this study, you can simply leave the game and request the study staff to help you out of the on-going experiment. If interested, the results of this study will be provided to you upon your request.

Risks and Discomforts

There is no side effect as a result participating in this study. However, if you feel discomfort by any mean during your participation in this experiment, you can ask study staff to take you off the study. Your condition may not worsen while participating in this study.

Confidentiality

Information gathered in this research study may be published or presented in public forums; however, your name and other identifying information will not be used or revealed. Medical records that contain your identity will be treated as confidential in accordance with the Personal Health Information Act of Manitoba. Despite the efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law.

All study documents related to you will bear only your assigned code and /or initials. Your data acquired during the games will be recorded and stored in computer files with your code. These data will be analyzed for the main purpose of study which is to investigate the human brain development and motor learning that lead to skilled human movement in terms of temporal and spatial accuracy. Students and researchers who will analyze your data will not have access to your identification and only know the files by their codes.

The University of Manitoba Health Research Ethics Board may review research-related records for quality assurance purposes. All records will be kept in a locked secure area and only those persons identified will have access to these records. If any of your medical/research records, need to be copied to any of the above, your name and all identifying information will be removed. No information revealing any personal information such as your name, address or telephone number will leave the University of Manitoba.

Voluntary Participation/Withdrawal from the Study

Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. You will not lose any benefits or care to which you are entitled upon the refusal to participate in or withdraw from the study.

We will tell you about any new information that may affect your health, welfare, or willingness to stay in this study.

Questions

You are free to ask any questions that you may have about your treatment and your rights as a research participant. If any questions come up during or after the study, contact the study doctor and the study staff: Dr. Zahra Moussavi at 204-474-7023. *Investigating Human's spatiotemporal perception using haptic computer games*

For questions about your rights as a research participant, you may contact The University of Manitoba Biomedical Research Ethics Board at (204) 789-3389. Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Statement of Consent

I have read this consent form. I have had the opportunity to discuss this research study with Dr. Zahra Moussavi and or his/her study staff. I have had my questions answered by them in language I understand. The risks and benefits have been explained to me. I believe that I have not been unduly influenced by any study team member to participate in the research study by any statement or implied statements. Any relationship (such as employee, student or family member) I may have with the study team has not affected my decision to participate. I understand that I will be given a copy of this consent form after signing it. I understand that my participation in this clinical trial is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that information regarding my personal identity will be kept confidential, but that confidentiality is not guaranteed.

By signing this consent form, I have not waived any of the legal rights that I have as a participant in a research study.

I agree to being contacted in relation to this study. **Yes** □ **No** □

Participant signature__________________________ Date ___________________

(day/month/year)

Participant printed name: ____________________________

__________________________ For Children Participants only ___________________________

Parent/legal guardian's signature (if applicable): ___________________

Date _________________

Parent/legal guardian's printed name (if applicable): __________________________

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their consent

Printed Name: ________________________ Date ___________________ (day/month/year)

Signature: ____________________________

Role in the study: _________________________

Appendix B. Questionnaires

B.1 Montreal Cognitive Assessment (MoCA)

MoCA is designed as a rapid screening instrument for mild cognitive dysfunction. It assesses different cognitive domains such as the followings:

- Attention
- Concentration
- Executive functions
- Memory
- Language
- Visuoconstructional skills
- Conceptual thinking
- Calculations
- Orientation

Administering the MoCA for cognitively healthy people takes about 10 minutes. The total possible score is 30 points; it is calculated by the sum all sub-scores with adding one point for an individual who has 12 years or fewer of formal education. A final total score of 24 and above is considered normal.

B.2 VRN's Pre- and Post-test Questioner

Pre-Test

Please share with us you experience with:

(a) Computers,

Never	Rarely	Sometimes	Often	Most of the Time

(b) Computers games,

Never	Rarely	Sometimes	Often	Most of the Time

(c) Virtual reality games

Never	Rarely	Sometimes	Often	Most of the Time

Post-Test

Did you use a strategy to perform the test? Yes/No

Pick the strategy that best describes how you found the target(s) in the test:

- Imagining yourself inside the building in a first person perspective, you aligned yourself with your direction before entering the house , planned in advanced to take right or left turn(s) once on the correct floor and remembered the number of left / right turns

- Using a bird's eye view for finding the target inside the house, you encoded the position of the target window in regard to the entrance of the building or entrance to each floor , and aligned yourself with the entrance of building

If you used any other strategy or cue , please explain :

Appendix C. Videos and Executable File

- A Sample Trial of VRN test (without House Rotation)
- A Sample Trial of VRN test (with House Rotation)
- Executable program of the VRN test