COGNITIVE FACTORS ASSOCIATED WITH INCREASED FALLS RISK IN SENIORS

by

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ABSTRACT

Falls are experienced annually by approximately one third of community dwellers over the age of 65, and while neuro-cognitive deficits have been shown to increase falls risk, the specific nature of these deficits remain unspecified. Here we examined whether visual-spatial attention may be a core neuro-cognitive system showing abnormal function in fallers. Using a between-groups design, we recorded event-related potentials in a canonical spatial cuing task performed by two groups of senior (aged 65 years old and older) participants: those with a recent history of falls and those with no such history. In terms of attentional control systems in cortex, we found no significant differences in function between groups. However, in terms of attentional facilitation of cortical processing, we found that fallers manifest specific abnormalities in the sensory/perceptual processing of targets in the left visual field. Our findings thus suggest that fallers have specific deficits in visuocortical systems associated with attentional enhancement of events on the left side of visual space.

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CO-AUTHORSHIP STATEMENT

The paper on which this thesis is based, has been accepted for publication in *Neuropsychologia*, co-authored by L.S. Nagamatsu, T.Y.L. Liu-Ambrose, P. Carolan, and T.C. Handy. L.S. Nagamatsu was primarily responsible for the identification and design of research program, performing the research, data analyses, and manuscript preparation. L.S. Nagamatsu prepared the remainder of this thesis.

1 INTRODUCTION

1.1 Falls risk in seniors

Falls in seniors are a major cost to society, both in terms of the health of our aging population as well as direct medical expenditure. Indeed, approximately 30% of community-dwellers over the age of 65 experience one or more falls per year (Tinetti, Speechley, & Ginter, 1988); 20% of these require medical attention, and in Canada, falls result in over 2.4 billion dollars per annum in health care costs (The Hygeia Group, 1998).

While falls are commonly attributed to physical problems, such as impairments in gait or balance, recent research has provided evidence suggesting that cognitive factors also play a role in falls risk. In fact, 60% of those with cognitive impairment fall annually; this is twice the rate of those without cognitive impairment (Tinetti, Speechley, & Ginter, 1988). While this relationship has been established using global measurements of cognition (Anstey et al., 2006), such as the Mini-Mental State Examation (MMSE), the specific components of cognition that may play a role in falls risk have just begun to be identified. Thus, my primary research aim is to identify the specific cognitive contributors to falls risk in seniors.

1.2   Cognitive contributors to falls risk

1.2.1   Executive functioning

One aspect of cognition that may be involved in falls is executive functioning. Reduced executive functioning has been found to be associated with falls (Anstey et al., 2006; Hausdorff et al., 2006). Anstey et al. (2006) found MMSE and verbal reasoning at baseline predicted falls over an 8-year period, and that declines in verbal ability, processing speed, and memory were also associated with falls. Holtzer et al. (2007) report that executive functioning was associated with both single and recurrent falls. In addition, impaired executive functioning has also been found to be associated with increased physiological falls risk such as impaired balance, gait, balance recovery, and reduced obstacle avoidance (Liu-Ambrose, Pang, & Eng, 2007). Along this line of research, it seems that there are specific cognitive processes related to the occurrence of falls, and that different processes are involved depending on whether you are looking at single falls versus recurrent falls. This idea is reinforced by a recent paper by Anstey and colleagues (2009), where those who experienced a single fall were more similar to non-fallers, compared to those who experienced multiple falls, on several tests of cognitive function. The authors concluded that while single falls may be related to subtle declines in executive control, multiple falls are associated with more widespread, generalized cognitive decline.

Recent research by Liu-Ambrose et al. (2008) investigated the neural correlates associated with decreased executive functioning in fallers versus age-matched controls. Using the Ericksen Flanker task, we found reduced activation in the right cerebellum of fallers during incongruent, relative to congruent, trials. Given recent evidence that the cerebellum is not only associated with motor movements, but also the integration of higher processes, such as executive functioning (Frings, Maschke, & Timmann, 2007; Timmann & Daum, 2007), our findings support the idea that impaired executive functioning may lead to increased falls risk, and suggests that the cerebellum may be a key link between executing functioning, motor abilities, and falls.

1.2.2 Visual-spatial attention

A second aspect of cognition that may play a key role in falls risk, is visual-spatial attention. Attention is essential for successful navigation and safe mobility through the environment. For example, one investigation of this relationship found that poor cognitive functioning, which is a risk factor for falls, was associated with decreased attention to the lower visual field (DiFabio et al., 2005). To date, however, there have been no systematic studies linking visual attention and falls risk. Specifically, the study by DiFabio et al. (2005) focused on low versus high functioning seniors, without directly assessing falls risk or falls history. Furthermore, there have been no functional neuroimaging studies in senior fallers prior to the work presented in this thesis.

1.2 Summary

Based on the above literature review, it is clear that cognitive factors contribute to falls risk in seniors. The challenge to identify the key components related to falls remains. Current evidence suggest that both executive functioning and visual-spatial attention appear to be important for understanding the relationship between cognition and falls, although the mechanisms behind how these factors may lead to increased incidences of falling is unclear. This thesis will focus on examining visual-spatial attention in senior fallers.

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2 ARE IMPAIRMENTS IN VISUAL-SPATIAL ATTENTION A CRITICAL FACTOR FOR INCREASED FALLS RISK IN SENIORS? AN EVENT-RELATED POTENTIAL STUDY[1]

2.1 Introduction

Falls in seniors is a major health care concern due to the injuries and injury-related death associated with falling. Surprisingly, factors other than just peripheral musculoskeletal problems contribute to falls risk. Basic deficits in cognitive function have been shown to be associated with falls (Clark, Lord, & Webster, 1993; Tinetti, Speechley, & Ginter, 1988) although the specific nature of these cognitive impairments have remained unclear. Our paper here hypothesizes that one specific aspect of cognition that may be related to falls risk is visual-spatial attention.

Why might visual-spatial attention be involved? There are at least three key pieces of evidence that suggest that visual-spatial attention is an important aspect of cognition to explore as a factor involved in falls risk.

First, visual-spatial attention has been linked to motor functions in normals (Handy et al., 2005). While visual-spatial attention has traditionally been associated with the ventral, or "what" pathway (Posner, 1980), research has

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[1] A version of this chapter has been accepted for publication. Nagamatsu, LS., Liu-Ambrose, TYL., Carolan, P., and Handy, TC. (In press). Are impairments in visual-spatial attention a critical factor for increased falls risk in seniors? An event-related potential study. *Neuropsychologia.*

recently began to focus on its role in the dorsal, or "how" pathway using vision to guide actions (Handy et al., 2003, 2005; Handy & Tipper, 2007). This suggests that problems that lead to falls, such as trouble planning and guiding movements, may be caused by underlying impairments in visual-spatial attention.

Second, deficits in visual-spatial processing are frequently the first symptom to appear in older populations as an indicator of age-related illness. Specifically, deficits in spatial abilities are often the first non-memory cognitive function to be impaired in age-related neurological disorders associated with increased falls risk, such as Alzheimer's disease (Bagurdes et al., 2008; Drago et al., 2008). For example, Parasuraman et al. (1992) found visual-spatial deficits in patients with dementia of the Alzheimer type (DAT) using a spatial cueing paradigm. Additionally, Alzheimer's patients show deficits in the perception of motion (Rizzo & Nawrot, 1998), which is integral to safe movement through the environment.

Third, fallers may have a narrowed focus of attention compared to non-fallers. In a study by Liu-Ambrose et al. (2008), fallers were shown to have less interference than non-fallers induced by peripheral flankers in the Erikson Flanker task. These results were interpreted as fallers having a more narrowed, or direct, focus of attention, leading to less distraction from the peripheral flanking arrows. Collectively, these three pieces of evidence point towards visual-spatial attention as a clear candidate for cognitive deficits associated with falls risk in seniors.

There are two separate aspects of visual-spatial attention that may be impaired in fallers: attentional control and attentional facilitation. Attentional control is the orienting or directing of attention to a particular location in space (Green & McDonald, 2008). On the other hand, attentional facilitation is the increase in the visual sensory-evoked cortical response for a stimulus in an attended location (Mangun, Hillyard, & Luck, 1993). Given these two aspects of visual-spatial attention, the main question of our study is whether either or both attentional control and attentional facilitation are impaired in seniors with a recent history of falls. Specifically, do fallers show deficits in the ability to orient attention to begin with, or if they are able to direct their attention, is there a deficit in the perceptual/sensory benefit for the cued location usually observed among normals?

In the current study, attentional control and attentional facilitations were assessed in fallers and non-fallers using event-related potentials (ERPs) in a spatial cueing paradigm (Posner, 1980). Attentional control was assessed by examining the ERP components elicited by attention-directing cues. The anterior directing attention negativity (ADAN) reflects correlates of directing attention (Green & McDonald, 2008), while the early attentional directing negativity (EDAN) reflects comprehension of attentional cues (Harter et al., 1989; Hopf & Mangun, 2000; van Velzen et al., 2002). Second, attentional facilitation was assessed by examining the ERP components elicited by visual targets. Sensory aspects of attentional facilitation are measured by an increase in the amplitude of

the P1 and N1 components while cognitive aspects, such as expectancy, are measured by an increase in amplitude of the P3, Nd1, and Nd2 components for unexpected targets relative to expected targets. Given the importance of identifying falls risk factors, our primary aim was to determine whether there are impairments in fallers in terms of attentional control, attentional factilitation, or both aspects of visual-spatial attention.

2.2   Methods

2.2.1   Subjects

Participants were a subset of senior women, aged 65-75 years, who participated in a 12-month prospective study examining the role of exercise on executive functioning. Women were used exclusively in this study due to differences in cognitive responses to exercise between genders (Colcombe & Kramer, 2003). Additionally, women are at greater risk for falls (Lord, Sherrington, & Menz, 2001). The incidence of falls was monitored throughout the 12-month study via monthly calendars.

Ten community-dwelling women who had experienced $\geq$ 2 minimal displacement non-syncopal falls in the previous six months prior to the study, aged 65-74 years (M = 69.8, SD = 3.16) participated in the study. One faller was left-handed and all had normal or corrected-to-normal vision. Fallers had on average 3 falls (SD = 1.25), ranging between 2 and 6 falls.

In addressing the question of possible visual-spatial attentional deficits in seniors with a history of falls, it is important to distinguish between impairments due to aging in general versus impairments specifically correlating with falls risk. Visual-spatial attention is relatively well preserved with age (Curran et al., 2001; Kok, 2000; Lorenzo-Lopez et al., 2002), although some notable differences between seniors and young controls have been found. Due to these reported age-related differences, our study included an age-matched control group of non-fallers as a normative reference. Ten community-dwelling controls, aged 66-74 years (M = 69.0, SD = 2.67) participated in the study. To be included in the "non-fallers" control group, individuals must not have experienced any minimal displacement falls (with or without syncope) in the previous six months prior to this study.

General inclusion criteria for all participants included an MMSE score $\geq$ 24 and visual acuity of at least 20/40 with or without corrective lenses. General exclusion criteria for all participants included those with neurodegenerative disease (e.g., Alzheimer's disease) and stroke, those who were currently taking psychotropic drugs, and those with a history indicative of carotid sinus sensitivity (i.e., syncopal falls). All participants provided written informed consent at the beginning of the study.

2.2.2 Descriptive measures

To reduce the number of possible confounding variables in the association between impaired visual attention and a recent history of falls, several descriptive

measures were obtained for all participants (Table 1). Global cognitive state was assessed using the Montreal Cognitive Assessment (MOCA), where the maximum score is 30 and higher scores indicate better performance. The Geriatric Depression Scale (GSD) was used to screen for depression, where a score of 11 and above indicates severe depression. General mobility was assessed by the Timed Up and Go Test (TUG), which instructs participants to rise from a standard chair with arms, walk a distance of three meters, turn, walk back to their chair and sit down again. Faster times indicate better performance. Physiological falls risk was assessed by the Physiological Profile Assessment (PPA) (Lord, Sherrington, & Menz 2001) which assesses vision, proprioception, strength, reaction time, and balance. A PPA z-score below 0 indicates low risk for falling, 0-1 indicates mild risk, 1-2 indicates moderate risk, and 2 and above indicates high risk. Cognitive performance of three central executive functions were assessed: 1) set shifting, assessed using Trail Making Test B; 2) updating (working memory), assessed using the digits forward and back tests; and 3) response inhibition, assessed using the Stroop Colour Word Test. Faster times on both Trail Making Test B and Stroop indicate better performance. Digits forward and back tests are measured by number of digits correctly completed.

2.2.3 Apparatus and stimuli

Stimuli were presented on an 18 inch colour monitor placed 100 cm from the subject. At the beginning of each trial, a fixation cross was presented in the centre of the screen for 1000 ms. Next, an arrow (1.26^{o} x 0.46^{o}) was presented

at fixation and cued either the left or the right target location. The cue remained

on the screen for the rest of the trial. The target, which was an "X" (0.92^o x

0.92^o), appeared 1000 ms (randomly jittered between 900 and 1100 ms) after the

on-set of the cue in either in the left visual field or the right visual field (target was

4.57^o from the top of the screen 11.31^o from the bottom of the screen, and 4.86^o

from the left/right edge of the screen) and remained on the screen until a

response was made. The arrow predicted the target location with 80% accuracy.

After the response, the next trial began immediately, with the presentation of the

next fixation cross.

2.2.4 Procedure

The task requires subjects to indicate via button presses whether the target

appeared in the right visual field or left visual field, as quickly and accurately as

possible. Participants were instructed to press one button with their left hand if

the target appeared on the left, and another button with their right hand if the

target appeared on the right. There were 12 blocks all together, each with 76

trials (60 cued, 12 uncued, 4 catch). Each block lasted approximately 4 minutes.

Subjects were told to keep their eyes on the central fixation point for the duration

of the experiment.

2.2.5 Electrophysiological recording and analysis

During task performance, electroencephalograms (EEG) were recorded from 32

active electrodes (Bio-Semi Active 2 system) evenly distributed over the head.

All EEG activity was recorded relative to two scalp electrodes located over medial-frontal cortex (CMS/DRL), using a second order low pass filter of .05 Hz, with a gain of .5 and digitized on-line at a sampling rate of 256 samples-per-second. To ensure proper eye fixation and allow for the correction and/or removal of events associated with eye movement artifacts, vertical and horizontal electro-oculograms (EOGs) were also recorded, the vertical EOG from an electrode inferior to the right eye, and the horizontal EOG from an electrode on the right outer canthus. Off-line, computerized artifact rejection was used to eliminate trials during which detectable eye movements (> 1°), blinks, muscle potentials, or amplifier blocking occurred. For each subject, ERPs were averaged into 3,000 ms epochs, beginning 1,500 ms before stimulus onset. Subsequently, all ERPs were algebraically re-referenced to the average of the left- and right-mastoid signals, and filtered with a low-pass Gaussian filter (10 Hz half-amplitude cutoff) to eliminate high-frequency artifacts in the waveforms. The resulting ERPs (on average, 456 cued and 432 uncued trials per subject) were then used to produce grand-averaged waveforms. Statistical quantification of ERP data was based on mean amplitude measures relative to a -200 to 0 pre-stimulus baseline.

In terms of statistical analysis, repeated-measures mixed-model ANOVAs were used, using unpooled error terms in order to account for potential violations of sphericity for factors having more than 2 levels (Handy, Nagamatsu, Mickelborough, & Liu-Ambrose, In press).

Behavioural analysis

Behavioural data (reaction times and accuracy) were analyzed using an ANOVA with factors of group (fallers vs. non-fallers), visual field (left vs. right), and cueing (cued vs. uncued).

Electrophysiological analysis

The two aspects of visual-spatial attention that we examined were attentional control and attentional facilitation. Based on previous work examining visual-spatial attention in seniors, delayed latencies for the P1, N1, and P3 components, as well as differences in ERP morphology, such as attenuated P1 and N1 amplitudes, have been established as normative for seniors relative to young adult controls (Curran et al., 2001). Therefore, time ranges and electrode sites for each component were chosen according to standard windows and locations for examining these components in seniors.

Attentional control can be separated into the control of covert attentional orienting, which is measured by the ADAN (Anterior directing attention negativity, Seiss et al., 2007) component to the cue, and the appreciation of the meaning of the symbolic cue, which is measured by the EDAN (Early directing attention negativity, Seiss et al., 2007) component to the cue. Both the ADAN and the EDAN were examined for sites that are ipsilateral versus contralateral to the cued visual field, with a greater negativity expected at electrodes contralateral to the direction of the cue compared to electrodes ipsilateral to the cued direction.

Therefore, for each component, effects involving factors of laterality and between-groups differences were examined, with results involving other factors being tangential to the focus of our study. Attentional control was analyzed using a mixed-model repeated-measures ANOVA with factors of group (fallers vs. non-fallers), visual field (left vs. right), and laterality (ipsilateral vs. contralateral to the cued visual field).

Attentional facilitation can be further separated into sensory aspects of target responses, measured as an increase in amplitude of the P1 and N1 components to targets, and cognitive aspects of target responses, measured as an increase in amplitude of the P3, Nd1, and Nd2 components to the targets. For the P1 and N1, between-groups effects were analyzed via a mixed-model repeated-measures ANOVA that had factors of group (fallers vs. non-fallers), visual field (left vs. right), cueing (cued vs. uncued), and laterality (ipsilateral vs. contralateral to the visual field of the target). The P1 and N1 components were examined for targets which were cued versus uncued, with an increased amplitude expected for attended targets relative to unattended targets. The analysis for cognitive components was the same as for sensory/perceptual components, excluding the factor of laterality. The P3, Nd1, and Nd2 components were examined for cued relative to uncued targets. As these components reflect expectancies, the amplitudes of the P3, Nd1, and Nd2 are larger for unattended targets versus attended targets. Results presented for attentional facilitation involved effects of

cueing and between-groups effects, with other factors being extraneous to the focus of our study.

2.3 Results

2.3.1 Descriptive measures

The mean scores and standard deviations for each of the descriptive measures are presented in Table 2.1.

Table 2.1
Descriptive Measures for Non-Fallers and Fallers

Measure	Non-Fallers[a]		Fallers[a]	
	Mean	SD	Mean	SD
Age[b]	69.00	2.67	69.80	3.16
MOCA	24.60	2.63	26.50	1.90
GDS	0.50	1.58	1.00	2.16
TUG[c]	6.44	1.58	5.99	0.60
ABC	91.38	14.32	94.16	5.96
PPA	0.04	0.56	-0.66	0.92
Digits forward	8.70	0.95	8.40	1.84
Digits backward	4.20	2.53	4.50	1.90
Trail B[c]	89.66	45.94	67.43	17.64
Stroop[c]	79.16	9.19	82.71	18.36

[a]n = 10 for each group. [b]Years. [c]Seconds.

Independent samples t-tests were done for each descriptive measure (SPSS 12.0) and indicated that fallers and non-fallers did not significantly differ on any of the descriptive variables, all *p* values > .05. Specifically, the fallers and non-fallers were equally matched on age, MOCA, depression level, mobility, physiological falls risk, balance, set shifting, updating, and response inhibition.

2.3.2 Behaviour

Mean reaction times and accuracy scores are shown in Table 2.2 as a function of group (fallers vs. non-fallers) and attentional condition (cued vs. uncued).

Table 2.2
Behavioural Results for Non-Fallers and Fallers

Condition	Non-Fallers[a]		Fallers[a]	
	Mean	SD	Mean	SD
Cued[b]				
Left	0.46	0.06	0.43	0.10
Right	0.43	0.06	0.43	0.10
Uncued[b]				
Left	0.50	0.05	0.50	0.12
Right	0.48	0.07	0.47	0.10
Accuracy[c]				
Left	0.60	1.07	1.00	1.56
Right	1.00	1.41	1.60	1.07

[a]n = 10 for each group. [b]Reaction times measured in seconds. [c]Number errors.

There were no significant differences in the reaction times or accuracy of fallers and non-fallers, $F(1,18) = 0.11$, $p = 0.74$. A significant main effect of cueing was found, $F(1,18) = 13.89$, $p < 0.01$, indicating reaction times were faster for cued relative to uncued trials. A significant main effect of visual field was also found, $F(1,18) = 8.20$, $p = 0.01$, indicating that participants were faster responding to targets in the right visual field compared to targets in the left visual field.

2.3.3 Electrophysiology

<u>Attentional Control</u>

The plots for the ADAN component are presented in Figure 2.1 and mean amplitudes are presented in Table 2.3.

Table 2.3
Mean Peak Amplitudes for Attentional Control for Non-Fallers and Fallers

Condition[a]	Non-Fallers[b]		Fallers[b]	
	Mean	SD	Mean	SD
ADAN				
Ipsilateral	0.69	0.61	0.09	1.08
Contralateral	0.56	0.56	-0.02	1.00
EDAN				
Isilateral	0.42	0.54	0.18	1.02
Contralateral	0.33	0.46	0.12	0.87

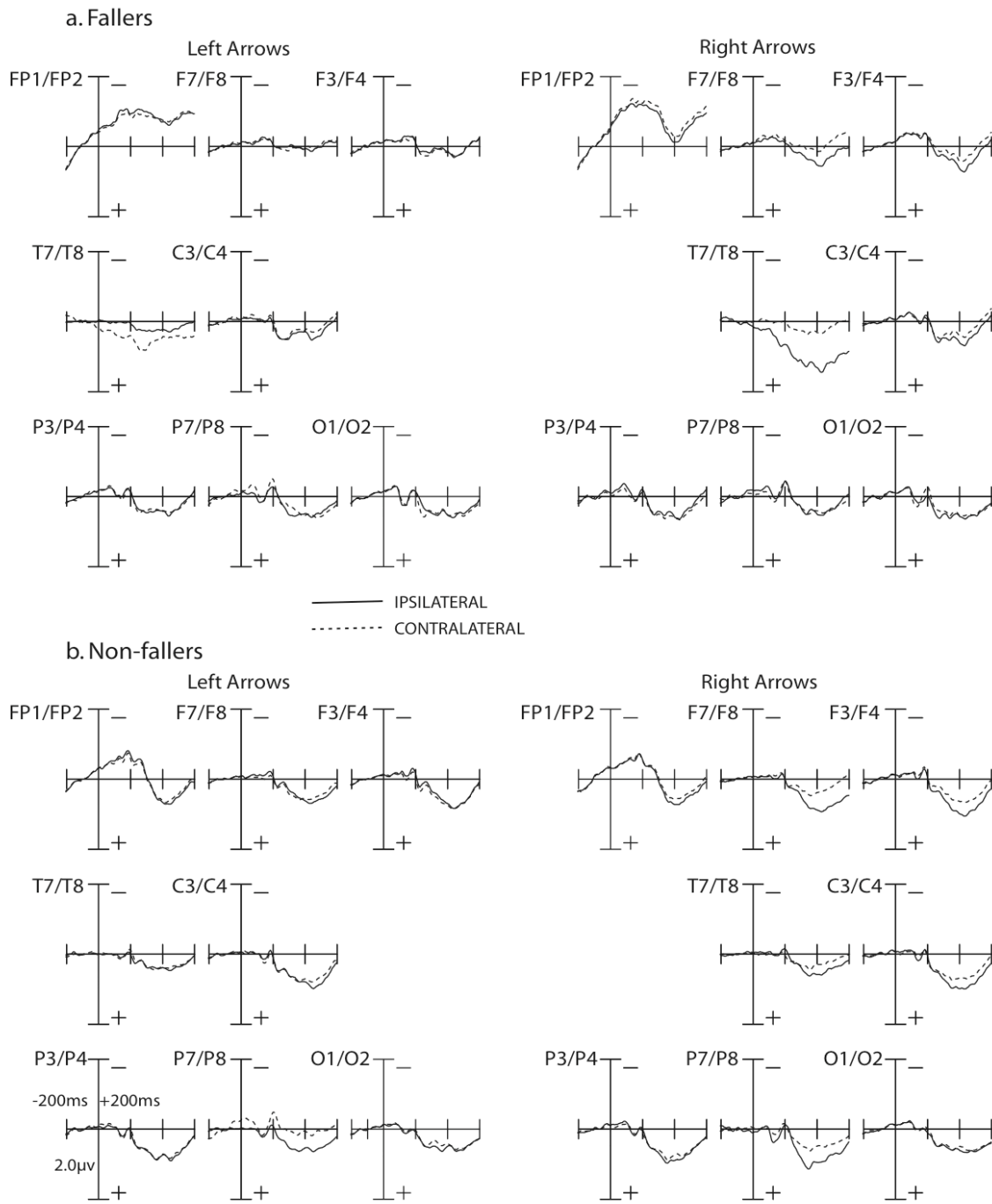[a]Peak amplitudes measured in uV. [b]n = 10 for each group.

Figure 2.1
Grand-averaged ERP waveforms for ADAN and EDAN components

The ADAN was examined at a time window of 310-440 ms post-cue at electrodes FP1, FP2, F7, F8, F3, F4, C3, and C4 (Jongen, Smulders, & Van der Heiden, 2007; Seiss et al., 2007; Talsma et al., 2005; van Velzen & Eimer, 2003). Between-group differences approached significance, $F(1,18) = 3.41$, $p = .08$. Specifically, there was a trend, where non-fallers tended to have a higher overall mean amplitude for the ADAN component, regardless of condition. Across all participants, the ADAN amplitude to cues was more negative in contralateral sites compared to ipsilateral sites to the visual field that was cued. This was confirmed by a significant main effect of laterality, $F(1,18) = 20.86$, $p < .001$. There was also a significant visual field by laterality interaction, $F(1,18) = 6.13$, $p = .02$, where the difference in amplitude between ipsilateral and contralateral sites was significantly greater in the right visual field than the left visual field.

The plots for the EDAN component are presented in Figure 2.1 and mean amplitudes are presented in Table 2.3. The EDAN component was examined at a time window of 200-400 ms post-cue at electrodes FP1, FP2, F7, F8, F3, F4, T7, T8, C3, C4, P3, P4, P7, P8, O1, and O2 (Jongen, Smulders, & Van der Heiden, 2007; Seiss et al., 2007; Talsma et al., 2005; van Velzen & Eimer, 2003). There were no significant between-groups differences, $F(1,18) = 1.22$, $p = .28$. The EDAN amplitude was more negative for cues in contralateral sites relative to ipsilateral sites to the cued visual field. This was confirmed via a main effect of laterality, $F(1,18) = 7.32$, $p = .01$. Additionally, there was a significant visual field by laterality interaction, $F(1,18) = 4.60$, $p = .05$. In the right visual field, ipsilateral

sites showed a larger EDAN amplitude than contralateral sites, but in the left visual field, the opposite pattern was observed with larger amplitudes in contralateral sites relative to ipsilateral sites.

Attentional Facilitation

Sensory/perceptual components

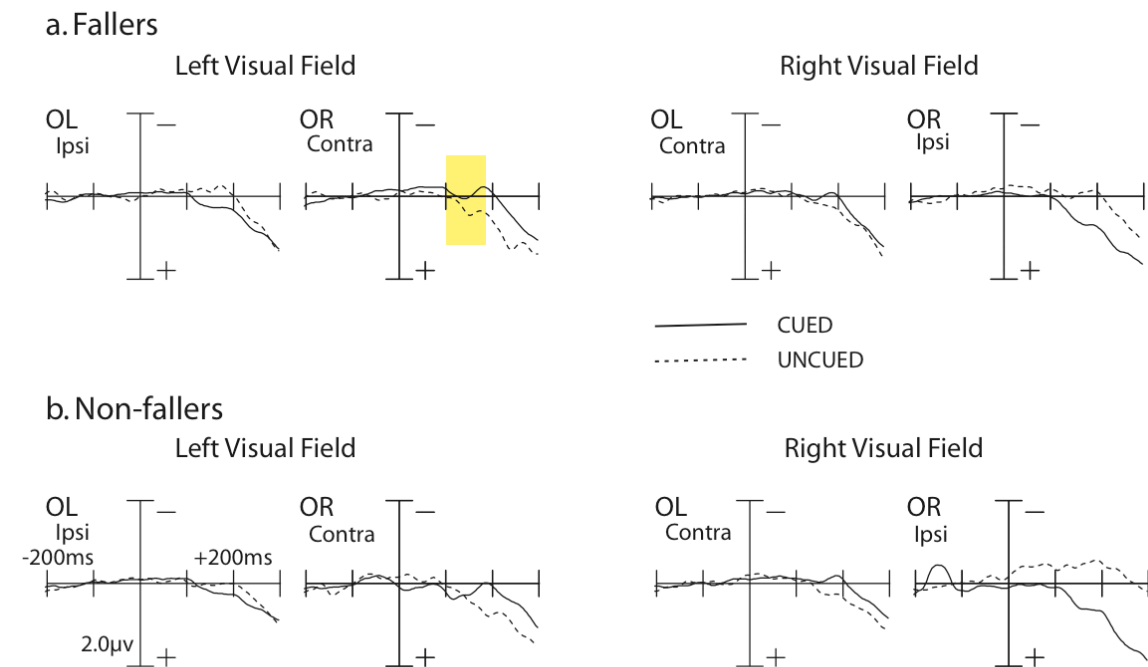The plots for the P1 component are presented in Figure 2.2 and mean amplitudes are presented in Table 2.4.

Figure 2.2
Grand-averaged ERP waveforms for P1 and N1 components

Table 2.4

Mean Peak Amplitudes for Attentional Facilitation for Non-Fallers and Fallers

Condition[a]	Non-Fallers[b]		Fallers[b]	
	Mean	SD	Mean	SD
P1				
Cued ipsilateral				
Left	0.03	0.12	0.10	0.21
Right	0.26	0.60	0.22	0.39
Cued contralateral				
Left	0.30	0.85	-0.04	0.35
Right	-0.10	0.25	-0.01	0.36
Uncued ipsilateral				
Left	0.02	0.34	-0.16	0.39
Right	-0.39	0.73	-0.07	0.56
Uncued contralateral				
Left	0.18	0.83	0.16	0.37
Right	-0.01	0.26	0.05	0.25
N1				
Cued ipsilateral				
Left	0.23	0.24	0.27	0.35
Right	0.62	1.24	0.65	0.63
Cued contralateral				
Left	0.10	0.85	-0.14	0.39
Right	-0.13	0.30	-0.02	0.55
Uncued ipsilateral				
Left	0.01	0.32	-0.17	0.60
Right	-0.51	0.88	-0.10	0.75
Uncued contralateral				
Left	0.60	0.75	0.42	0.58
Right	0.25	0.27	0.22	0.38
P3				
Cued	1.58	0.09	1.00	1.07
Uncued	2.44	1.07	3.01	1.46
Nd1				
Cued	0.30	0.38	0.48	0.58
Uncued	0.59	0.49	0.62	0.78
Nd2				
Cued	0.98	0.65	1.31	0.94
Uncued	1.48	0.82	1.69	1.06

[a]Peak amplitudes measured in uV. [b]n = 10 for each group.

The P1 to targets was analyzed looking at a time window of 100-150 ms post-stimulus at electrode sites OL and OR (Mangun & Hillyard, 1991). Across both groups of participants, when sites were ipsilateral to targets, the P1 amplitude was larger for cued trials compared to uncued trials, whereas when sites were contralateral to targets, the P1 amplitude was larger for uncued trials, replicating the P1 results in seniors from Curran et al. (2001). This was confirmed by a significant cueing by laterality interaction, $F(1,18) = 6.37$, $p = .02$. Between fallers and non-fallers, there was an effect of cueing by visual field. Specifially, the P1 amplitudes were different between fallers and non-fallers in contralateral sites to targets in the left visual field. This observation was supported by a significant group by visual field by cueing by laterality interaction, $F(1,18) = 4.79$, $p = .04$. This interaction was followed up by a within-groups analysis looking at fallers and non-fallers separately. Fallers showed a larger P1 amplitude in ispsilateral sites for cued targets relative to uncued targets and larger P1 amplitude in contralateral sites for uncued targets relative to cued targets in both visual fields, as confirmed by a significant cueing by laterality interaction, $F(1,9) = 10.41$, $p = .01$. In contrast, non-fallers showed a difference in the cueing by laterality interaction for the left versus right visual field. In the left visual field, the P1 amplitude was larger in both ipsilateral and contralateral sites to the visual field of the target for cued targets compared to uncued targets. In the right visual field, the P1 amplitude was larger in ipsilateral sites for cued targets relative to uncued targets, but larger in contralateral sites for uncued targets compared to

cued targets. This was confirmed by a trend towards a visual field by cueing by laterality interaction, $F(1,9) = 4.44$, $p = .06$ in non-fallers.

The plots of the N1 components can be seen in Figure 2 and mean amplitudes are presented in Table 4. The N1 was analyzed looking at a time window of 150-200 ms post-stimulus at electrode sites OL and OR (Mangun & Hillyard, 1991). No between-groups differences were found for the N1 component, $F(1,18) = 0.00$, $p = .97$. In the right visual field, N1 amplitudes were larger for cued trials relative to uncued trials whereas in the left visual field, N1 amplitudes were larger for uncued trials relative to cued trials, as confirmed via a significant visual field by cueing interaction, $F(1,18) = 6.13$, $p = .02$. When sites were ipsilateral to the targets, the N1 amplitude was larger for cued trials compared to uncued trials. When sites were contralateral to targets, however, the N1 amplitude was larger for uncued trials. This was supported by a significant cueing by laterality interaction, $F(1,18) = 54.28$, $p < .001$. These results suggest normal modulations of the N1 component for both fallers and non-fallers.

Cognitive/post-perceptual components

The plots for the P3 component can be seen in Figure 3 and mean amplitudes are presented in Table 4.
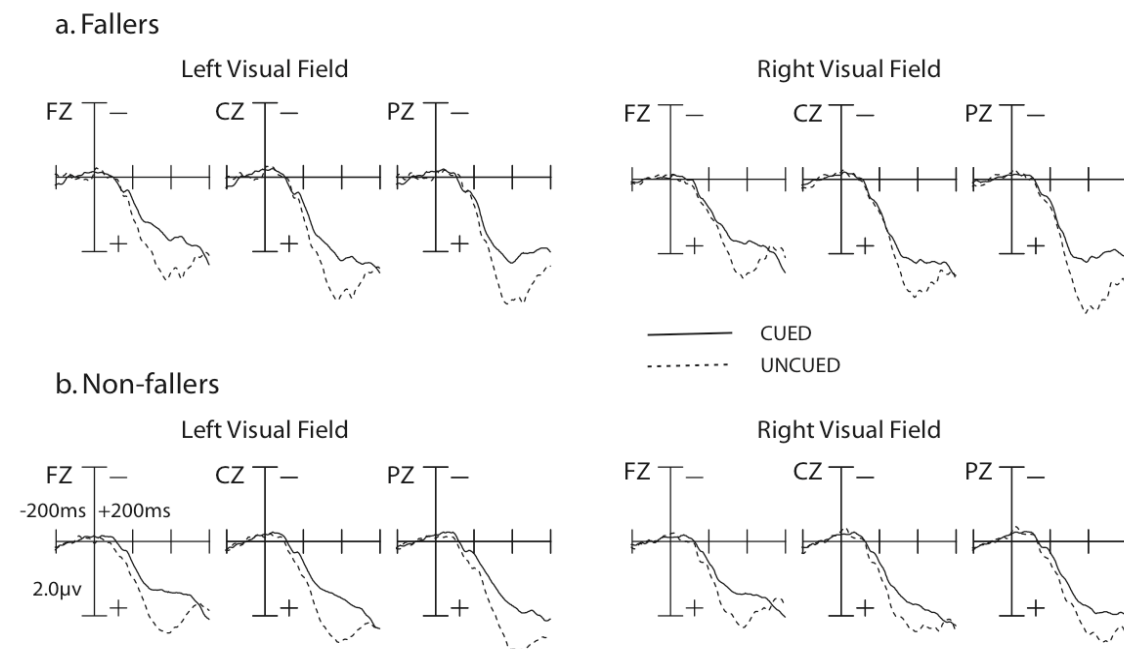
a. Fallers

Left Visual Field

Right Visual Field

FZ   CZ   PZ

FZ   CZ   PZ

CUED
UNCUED

b. Non-fallers

Left Visual Field

Right Visual Field

FZ   CZ   PZ

FZ   CZ   PZ

-200ms   +200ms

2.0µv

Figure 2.3
Grand-averaged ERP waveforms for the P3, Nd1, and Nd2 components

The P3 component was examined at a time window of 350-450 ms post-stimulus at electrode sites FZ, CZ, and PZ (Eimer, 1996; Eimer, 1998). No significant between-groups differences were found, $F(1,19) = 1.11$, *p* = .31.   Normal modulations of the P3 component were found for both groups (Curran et al., 2001; Eimer, 1996; Eimer, 1998), with larger amplitudes for the P3 component for uncued relative to cued trials, indicated by a significant main effect for cueing, $F(1,18) = 39.90$, *p* < .001.

The plots for the Nd1 component can be seen in Figure 3 and mean amplitudes are presented in Table 4. The Nd1 component was examined at a time window

of 150-200 ms post-stimulus at electrode sites FZ, CZ, and PZ (Eimer, 1996; Eimer, 1998). No significant between-groups differences were found, $F(1,18) = 0.24$, $p = .63$, but both fallers and non-fallers showed normal Nd1 modulations (Curran et al., 2001; Eimer, 1996; Eimer, 1998). Specifically, uncued trials showed a larger Nd1 amplitude than cued trials, confirmed via a significant main effect of cueing, $F(1,18) = 12.66$, $p < .01$.

The plots for the Nd2 component can be seen in Figure 3 and mean amplitudes are presented in Table 4. The Nd2 component was examined at a time window of 220-300 ms post-stimulus at electrode sites FZ, CZ, and PZ (Eimer, 1996; Eimer, 1998). No significant between-groups differences were found, $F(1,18) = 0.53$, $p = .48$, although both groups showed normal Nd2 modulations (Curran et al., 2001; Eimer, 1996; Eimer, 1998). A main effect of cueing, $F(1,18) = 23.84$, $p < .001$ was found, where uncued trials showed a larger Nd2 amplitude than cued trials.

2.4   Discussion

The goal of our study was to examine whether seniors with a history of falls show deficits in visual spatial attention relative to age-matched controls. In this regard, two aspects of visual-spatial attention were assessed: attentional control, which concerns the ability to orient attention to a particular location in visual space, and attentional facilitation, which concerns whether attentional orienting actually affects or modulates sensory/perceptual sensitivity at the attended location.

In terms of attentional control, fallers and non-fallers showed no significant differences in function in that both groups were able to direct their attention towards the cued location. This was indicated by the presence of ADAN and EDAN components in the ERPs elicited by cues. However, in terms of attentional facilitation, fallers showed impairments in the normal ability of attention to modulate visual sensory processing. Specifically, both groups showed increases in the amplitude of the P1 ERP component for attended vs. unattended targets in the right visual field. In contrast, for targets in the left visual fields, only non-fallers showed the normal attention-related increase in P1 amplitude. There were no group differences in terms of cognitive aspects of attention, such as expectancy, as indicated by normal modulation of the P3, Nd1, and Nd2 components in both fallers and non-fallers. Our results thus suggest that the difference between fallers and non-fallers is not in *generating* an attentional orienting response to begin with or later cognitive processing of the targets, but rather, in their ability for attention to *facilitate or enhance* visual processing in the left visual field.

That fallers may show impairments in spatial attention-related facilitation is consistent with our recent finding that fallers appear to have a narrowed focus of attention at fixation (Liu-Ambrose et al., 2008). To the point, we found that fallers showed reduced response interference in an Eriksen flanker task relative to age-matched controls, data suggesting that there was a reduction in attentional

processing of distractors distal to the target at fixation. Our current findings expand our understanding of spatial attention deficits in fallers by demonstrating that this population also appears to have a reduced ability to facilitate perceptual processing when attention is oriented to the left side of visual space. Given this conclusion, at least two key questions follow.

First, why might visual-spatial attention only be impaired in the left visual field of fallers? Several converging lines of evidence suggest that the left visual field is particularly susceptible to attentional deficits from neurological conditions or disorders. For example, patients with unilateral visual neglect are more likely to manifest neglect in the left visual field relative to the right (Bublak, Redel, & Finke, 2006; Reuter-Lorenz, Kinsbourne, & Moscovitch, 1990). Why? Visual-spatial attention studies with split-brain patients suggest that the attentional bias in the right hemisphere is the result of the two hemispheres working independently to orient attention (Mangun et al., 1994). While the right hemisphere appears capable of orienting attention to both sides of visual space, the left hemisphere orients exclusively to the right visual field. As a consequence, whereas damage to the left hemisphere leaves the right hemisphere still capable of orienting to both the left *and* right side of space, damage to the right hemisphere leaves the left hemisphere *only* orienting to the right side of space. The importance of understanding this relationship between spatial attention and cerebral hemispheres is that our data here would thus

suggest that the basis for neurocognitive deficits in fallers may be right hemisphere specific.

Second, if fallers have impaired visual-spatial attention in the left visual field, how might this lead to falls? We suggest that attentional deficits may lead to falls in both *direct* and *indirect* ways. First, these deficits may lead to falls directly by causing one to fail to notice something immediately relevant for falls-avoidance. For example, it has been hypothesized that falls risk may be associated with abnormalities in attentional abilities in the lower visual field (Di Fabio et al., 2005), indicating that decreased attention to objects located on the ground, such as a step, may pose as potential fall hazards. While our study investigated attention in the left versus right visual fields, future studies will examine attention in the upper versus lower visual fields to further consider the role of visual-spatial attention in falls.

At the same time, indirect links between visual-spatial attention and falls may stem from a lack of motor coordination with the hands and vision. Visual-spatial attention has been shown to be integral for the planning of object-related actions, such as grasping objects (Handy et al., 2005). There are hand-related objects in the environment that aid in successful movement and vision is integral for their proper implementation. For example, an impairment in the ability to use vision to accurately judge the distance of a handrail may result in a fall, or the inability to properly organize one's hand configuration to grasp a handrail to either steady

oneself when negotiating stairs or catch oneself when actually starting to fall. While it is clear that there are both possible direct and indirect factors linking falls and visual-spatial attention, further studies are necessary in order to determine the exact mechanisms leading to falls.

In closing, there are two additional issues worth noting regarding how we have interpreted our results. First, although a between-group difference in the ADAN ERP component approached significance (P = 0.08), we interpreted this result as suggesting that there were no between-group differences in attentional control. While we recognize that the absence of significance may be power-related due to small sample sizes within each group, the pattern of results for attentional control were nevertheless inconsistent with the between-groups effect we found for attentional facilitation. Specifically, differences in attentional facilitation between fallers and non-fallers were in the left visual field. If fallers did have impairments in attentional control, we would expect to see a similar pattern of results. Instead, fallers showed a difference in overall amplitude for the ADAN, rather than visual field or laterality differences. Based on this inconsistency between the patterns of results, we have thus reported normal attentional control for fallers.

Second, there were notable differences in attentional facilitation effects as identified via P1 vs. reaction time measures. In particular, we report that fallers have impaired attentional facilitation in the left visual field as indicated by the P1

ERP component, yet there were no corresponding differences between fallers and non-fallers, as measured by reaction times. That is, both groups showed normal attentional effects in reaction times, with responses faster for cued relative to uncued targets. In hindsight, this result is perhaps not surprising. For one, behavioural effects of attention have been previously found without corresponding effects in the P1 (e.g., Handy & Khoe, 2005), indicating that attention can differently affect reaction times and visual sensory gain. For another, the finding is consistent with the hypothesis that the two measures may reflect different underlying processes. For example, sensory gain effects captured in the P1 may be more important for vision-for-action whereas reaction time effects may be more central to vision-for-perception (e.g., Handy et al., 2003; Handy et al., 2005). Indeed, that fallers—who have problems in the motor domains—showed selective deficits in sensory gain is certainly consistent with this possibility.

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3 CONCLUSION AND FUTURE DIRECTIONS

3.1 Summary

Based on the study presented above, fallers have impaired sensory gain in the left visual field. Specifically, we found that fallers do not have the same sensory benefits as non-fallers, as indexed by the P1 component. Importantly, fallers did not show any deficits in terms of attentional control – they exhibited normal abilities to direct their attention, as measured by the EDAN and ADAN components time-locked to cues. This leads to the interpretation that while fallers are able to initially orient their attention to a particular area in visual space, they do not experience an increased sensory sensitivity at the attended location.

3.2 Impairments in visual-spatial attention

3.2.1 Visual-spatial attention in seniors

General cognitive decline has been well documented in seniors (e.g., Flicker et al., 1993; Koss et al., 1991; Nettelbeck & Rabbitt, 1992), including problems specifically associated with visual-spatial attention (Curran et al., 2001; Kok, 2000; Lorenzo-Lopez et al., 2002). Previous work has found delayed latencies in the P1 component in seniors (e.g., Curran et al., 2001), leading to the interpretation that seniors have slower visual processing compared to young controls. Current work by Nagamatsu et al. (manuscript in preparation), however, found that seniors not only have an increased latency for attentional facilitation in the left visual field, but they also have reduced attentional control in the left visual field. Given that lower attentional selection results in a reduced, or

even absent, attentional facilitation response (Jongen et al., 2007), our findings thus suggest that the deficits in visual-spatial attention experienced by seniors is attributed to an attenuated ability to direct attention in visual space, which then leads to a reduced sensory facilitation effect. In order to properly interpret results from our senior fallers, it is important to first understand differences in visual attention with aging. That is, it is critical to appreciate that our reference group (i.e., senior non-fallers) may differ from the normative reference group (i.e., young controls).

3.2.2 Visual-spatial attention in fallers

Given the importance of attention in safe mobility and navigation in the environment, it is not surprising that fallers show specific deficits in this domain. The above research presented in this thesis suggests that fallers, unlike seniors in general, are specifically impaired in attentional facilitation. Determining which aspect(s) of attention are relevant to falls will help us to understand the mechanisms linking the two, and will guide future treatment and prevention strategies. For example, depending on whether attentional deficits are occurring early versus late in processing will guide the treatment programs that are developed.

3.2.3 Visual-spatial attention in other clinical populations

Lastly, understanding the full extent of the impairments in visual-spatial attention experienced by seniors can provide critical insight into age-related disorders associated with attention. Given that deficits in spatial ability is among one of the

first symptoms to manifest in age related disorders, such as Parkinson's and Alzheimer's, and that patients with these disorders are more likely to experience a fall (Baguardes et al., 2008; Drago et al., 2008), understanding the relationship between aging and attention may provide us with key intervention or treatment strategies.

3.3 Limitations

3.3.1 Sample sizes

Working with a specific population is difficult because subjects who are eligible to participate are limited. Therefore, our previous studies have had relatively low sample sizes. While we have been able to find significant and strong results with our low sample sizes, increased sample sizes may allow us to find more subtle differences between groups that were not previously possible.

3.3.2 Defining "fallers"

One last limitation of our research is the definition of our population of interest – i.e., fallers. To begin with, a fall can be a subjective definition. In order to avoid ambiguity, the current study described above uses the Kellogg definition of falls (Kellogg International Work Group, 1987): "unintentionally coming to the ground or some lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke or an epileptic seizure." In addition, seniors are subject to retrospective bias when asked to recall the occurrence of falls. Therefore, the strength of our research

comes from the use of monthly falls calendars, where participants record and report falls as the happen. This provides a more detailed and accurate account of each fall.

3.4   Future directions

3.4.1 Exogenous attention in fallers

We have already demonstrated that fallers have trouble with detection of objects in an environment location that they are consciously attending to, but what about objects that may appear in an unattended location?   That is, are their impairments specific to controlled attention, or is it possible that fallers also show deficits in terms of reflexive orienting of attention as well?

The next phase of my research will involve examining reflexive, or exogenous, attention in senior fallers. There will be two key stages to this upcoming project: 1. Basic laboratory paradigms used to assess reflexive orienting, and 2. A "real-life" experiment using virtual reality equipment to simulate a street-crossing experience.   I expect that fallers will show deficits in reflexive orienting, specifically in the left visual field. For example, fallers may be less likely to notice hazards or obstacles suddenly appearing in the periphery. This research will help us to understand the extent of the deficits in attention experienced by fallers.

3.5   Significance of research

Identifying visual-spatial attention differences between senior fallers and non-fallers refines the focus of future research in the area of cognition and mobility and in turn, leads to the refinement and development of behavioural, cognitive, or neuropharmacological interventions for effective falls prevention. Effective prevention strategies would not only reduce injuries and death at the individual level but also reduce health care costs at the societal level. Also, my findings could be applied to develop novel falls risk screening strategies.

3.6   Applications of research

Establishing a connection between falls and visual-spatial attention will eventually lead to screening tools and treatment strategies.

3.6.1   Screening tools

Identifying a "falls signature" will allow us to assess falls risk in individuals prior to the onset of recurrent falls. For example, demonstrating that an absent P1 ERP response in the left visual field is highly predictive of future falls-related problems would allow us to easily test older adults in the laboratory to identify those at risk for falling and intervene before falls becomes an issue.

3.6.2 Treatment strategies

Once seniors are either identified as being high-risk for falling or already have experienced recurrent falls, future falls may be prevented through cognitive training. If visual-spatial attention is demonstrated as a contributing factor, directly leading to falls, improving visual-spatial attention may lead to a reduction, or lower risk, of falls. For example, recent research has been done using action video games to train participants to increase visual attention abilities (Achtman, Green, & Bavelier, 2008).

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