# Health & Fitness Journal of Canada




**Volume 11** **September 30, 2018** **Number 3**

**ORIGINAL ARTICLE**

# A Six-Month Study of Antisaccade Reaction Time in Elderly Adults with Cognitive Impairment in a Retirement Living Home: A Mind Fun Sub-Study

**Erin M. Shellington[1], Matthew Heath[1], Andrea F.M. Petrella[1,] Dawn P. Gill[2,] Robert J. Petrella[1,2]***


## Abstract

**Background**: Oculomotor control assessed via the antisaccade task has shown to be sensitive to change following exercise programs in older adult populations. The antisaccade task has been shown to be associated with executive function. However, this task has not been assessed in adults over 80 years of age. **Purpose:** The purpose of this investigation was to determine the feasibility of the antisaccade task in octogenarians over a 6-month period and determine if any change in reaction time (RT) occurs. **Methods**: The subjects participated in a 12-week Square-stepping exercise (SSE) program (over a 6-month period). The feasibility and change of an executive-related oculomotor task required participants to look mirror-symmetrical to a target (i.e., antisaccades), which were assessed at baseline and post-intervention. **Results**: Seven adults (85.4 years old, SD=3.2; Montreal Cognitive Assessment score of 22.6, SD=3.5) out of a larger cluster of 71 completed assessments at baseline and post-intervention. Results showed no reliable change in antisaccade RT from baseline (360 ms, SD=37) to post-intervention (361 ms, SD=40); however, a decrease in RT variability was observed during this time frame (i.e., baseline: 23 ms, SD=12; post-intervention: 15 ms, SD=13). **Conclusions**: Oculomotor assessments have limited feasibility in elderly adults with cognitive impairment due to age-related eye disease. Furthermore, our results demonstrated maintenance of executive control and improved post-intervention planning stability in an elderly population at risk for further cognitive decline; further investigation with a control group is required. **Health & Fitness Journal of Canada 2018;11(3):3-11.**


*Keywords:* Eye Tracking, Executive Function, Exercise, Older Adults, Oculomotor Control

From [1]School of Kinesiology, Faculty of Health Sciences, University of Western Ontario, London Canada; [2]Department of Family Medicine, Schulich School of Medicine and Dentistry, University of Western Ontario, London Canada; *Corresponding Author; email: Robert.Petrella@schulich.uwo.ca, address: 2102 Western Centre for Public Health and Family Medicine, 1465 Richmond St. Western University, London ON, N6G 2M1; t. 519-661-2111 x 22119; f. 519-858-5029

## Introduction

Elderly[1] adults with objective cognitive impairment in retirement living (RL) homes are at high risk of further cognitive decline (Canadian Institute for Health Information (CIHI), 2011; Sperling et al., 2011). Evidence has shown that exercise programs involving aerobic and/or resistance training can improve cognitive function and brain health in adults with and without objective cognitive impairment (Erickson et al., 2011; Liu-Ambrose et al., 2012; Nagamatsu et al., 2013), including those living in RL homes (Brown et al., 2009).

The antisaccade task is an objective and non-invasive measure requiring that an individual look (i.e., saccade) mirror-symmetrical to the location of a target stimulus. Due to the non-standard nature of antisaccades, directionally correct task performance has been tied to the activation of prefrontal cortical regions involved in executive-related cognitive control (for review see (Everling and Johnston, 2013; Munoz and Everling, 2004)). Antisaccade reaction time (RT) increases with increasing age (Munoz, et al., 1998), and is a finding taken to evince less effective executive control with

[1] In this manuscript, elderly refers to octogenarians, as opposed to older adults (adults less than 80 years of age).

advancing age. Moreover, because executive control is one of the first domains effected in dementia, the resolution of the antisaccade task has shown promise in detecting subtle declines in executive function that may not be detected in paper and pen based tests (Peltsch, et al., 2014). It is, however, important to recognize that antisaccade performance is not well studied in adults above the age of 80 years, and therefore, more data is required in this growing population to better understand cognitive – and executive-specific – changes in octogenarians.

The prefrontal networks supporting antisaccades show enhanced task-specific activity in both young and older adults following a long-term exercise program (Colcombe et al., 2004). Moreover, our group showed that a six-month moderate-intensity aerobic exercise or multi-modality exercise program improves antisaccade RT in community-dwelling older adults (average ages 65 - 72 years) with subjective or objective cognitive impairment. In other words, a long-term exercise program improves executive-related oculomotor control in persons at increased risk of cognitive decline (Heath et al., 2017; Heath et al., 2016).

The present study was a sub-study of a larger pilot cluster randomized controlled trial (RCT) in RL and long-term care homes in Ontario Canada, in which we proposed that the use of a novel cognitive training program, called Square-stepping exercise (SSE). The SSE program is a visuospatial working memory task with a cued stepping response (i.e., cognitive training program with a physical component). The program is progressive, and it increases in complexity as a visuospatial task. Additionally, it is performed in a group-based environment that promotes social interaction. Importantly, SSE has been shown to produce improved memory, executive

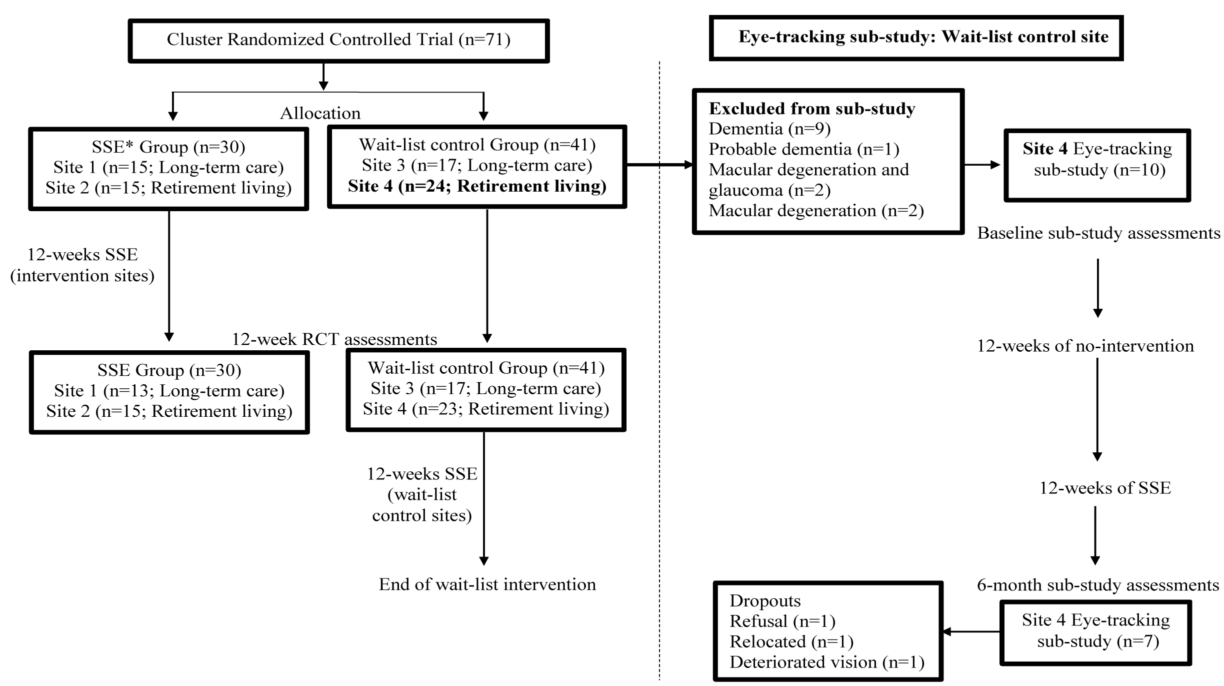


**Figure 1**: Study flow diagram for eye-tracking sub-study. Left: represents study flow for larger randomized trial. Right: represents study flow for eye-tracking sub-study. *SSE = Square-stepping exercise

function, and global cognitive functioning in community-dwelling older adults (Gill et al., 2016; Teixeira et al., 2013).

To our knowledge, there are no reports of antisaccade performance in octogenarians with objective cognitive impairment, nor have there been reports of the effect of SSE on executive control in this population. In this study, a 12-week cognitive training intervention was employed to assess whether antisaccade RT changes over time in this population. This report therefore represents a unique population of executive-related oculomotor functioning to the literature to further advance our knowledge on cognition and aging.

Our primary aim was to determine whether an assessment of oculomotor function was feasible in octogenarians living in RL homes, determined by eligibility for the assessment (i.e. no eye-related disease and adequate perimetry). The secondary aim was to assess whether a 12-week SSE intervention improves executive-related oculomotor control in octogenarians living in RL over a six-month period.

## Methods

### *Participants*

The participants of the larger cluster RCT (n=71) were recruited to participate in this sub-study. In the current study, the participants were in a RL home in Kitchener Canada, which was randomized as a wait-list control site (n=24). Participants were pre-screened (using perimetry) and excluded if they had known eye-related issues associated with older age, such as macular degeneration and glaucoma – eye diseases that preclude accurate eye-tracking (Figure 1). A total of ten participants were eligible and agreed to participate; seven completed both baseline and post-intervention assessments (1 refused due to recent familial death, 1 moved, and 1 had deteriorated vision, specifically macular degeneration progressed to interfere with stable eye tracking, and therefore could not be tracked). Data presented in this paper are for the seven participants who competed both assessments. Participants were assessed at baseline, (21 July 2016, 11 August 2016) and post-intervention (9 or 10 February 2017).

All participants provided written informed consent approved by the Western Health Sciences Research Ethics Board (No.107891) and this study complied with the Declaration of Helsinki of 1975.

### *Intervention*

The SSE intervention was conducted twice weekly for 45 minutes over 12-weeks (November 2016 to February 2017). An instructor demonstrated a stepping pattern across a gridded mat; the mat is 250 cm x 100 cm and it is divided into four columns of 10 rows, totaling 40 squares. The participants were required to memorize and repeat the patterns correctly two times. There are over 200 patterns that are progressive; the SSE program begins with beginner patterns and gradually progresses to intermediate and advanced patterns. The number of steps in a pattern ranges from two to 16 steps, and includes stepping forward, backward, horizontal or diagonal in direction to challenge and potentially improve visuospatial, and executive skills. Each pattern has a right and left foot start. SSE is a group-based program and participants are encouraged to support one another and provide peer support, therefore SSE increases social engagement.

### *Oculomotor Assessment*

Participants sat in a height adjustable chair placed in front of a table with their head in a head/chin rest and viewed a 30-inch LCD monitor (1280 by 960 pixels, DELL 3007WFP, Round Rock, TX, USA) located at their midline and 550 mm from the edge of the table. The gaze position of the participants' left eye was assessed using a video-based eye-tracking system, sampling 360Hz (Eye-Trac6; Applied Sciences Laboratories, Bedford, MA, USA). All computer events were controlled via MATLAB (v. 7.6; MathWorks, Natick, MA) and the Psychophysics ToolBox extensions (v. 3.0; Brainard 1997).

For all trials, a central fixation (i.e., 1° cross) was presented and following the attainment of a stable fixation (+1.5° for 450 ms), a 1,000-2,000 ms randomized foreperiod was initiated during which time participants maintained their fixation. At the end of the foreperiod, a target was briefly (i.e., 50 ms) presented 10.5° (i.e., proximal) and 15.5° (i.e., distal) left and right of the fixation and in the same horizontal meridian as the fixation cross. The onset of the target cued participants to pro- (i.e., saccade to the direction of the target) or antisaccade (i.e., saccade mirror-symmetrical to the target) as quickly and accurately as possible. The fixation cross was occluded co-incident with offset of the target stimulus (i.e., overlap paradigm). Pro- and antisaccades were completed in separate and randomly ordered blocks with 10 trials completed to each visual field (i.e., left and right of fixation) and target eccentricity combination.

### *Statistical Analysis*

Data reduction and statistical analyses were completed MATLAB (v. 7.6), and SPSS (v. 23), respectively. Data post-processing were in line with an extensive number of studies completed by our group (Heath et al., 2017). We examined mean pro- and antisaccade RT and associated RT variability (i.e., within-participant standard deviations) via 2 (time: baseline, post-intervention) by 2 (task: pro-, anti-saccade) repeated measures ANOVAs. The same ANOVA model was used to examine participant-specific RT skewness scores. We examined skewness to determine whether pro- and antisaccade RT distribution symmetries differed from baseline to post-intervention. Significance was determined at $p=0.05$.

## Results

Participants were 86% female, mean age 85.4 years (SD 3.2; range 79-89) with subjective and objective cognitive impairment, mean Montreal Cognitive Assessment (MoCA) score 22.6 (SD 2.5; range 18-25) out of 30 with an average of 14.4 (SD 2.8) years of education (Table 1).

**Table 1: Participants baseline characteristics, n=7.**

| | |
|---|---|
| **Female sex,** No. (%) | 6 (86) |
| **Age, years,** mean(SD) | 85.4 (3.2) |
| **Caucasian,** No. (%) | 7 (100) |
| **Years of education,** mean (SD) | 14.4 (2.8) |
| **Height (cm),** mean (SD) | 161.8 (9.6) |
| **Weight (kg),** mean (SD) | 68.7 (10.1) |
| **Blood pressure, mmHg,** mean (SD) | 128.9/69.7 (5.4/7.6) |
| **Number of Medications,** mean (SD) | 8.3 (2.9) |
| **Number of Diagnoses,** mean (SD) | 4.9 (4.5) |
| **Montreal Cognitive Assessment /30,** mean (SD) | 22.6 (2.5) |
| **Do you feel your memory and/or thinking skills have gotten worse recently? (yes or no),** No. (%) | 7 (100) |
| **Are you concerned/worried about your worsening memory and/or thinking skills (yes or no),** No. (%) | 4 (57) |

***Baseline and post-intervention oculomotor assessment***

The analysis of RT revealed a main effect of task, $F(1,6)=27.12$, $p<0.01$, indicating that prosaccade values (255 ms, SD=48) were shorter than antisaccades (360 ms, SD=37). Notably, Figure 2 shows that neither the effect of time nor the time by task interaction was significant, $Fs(1,6)<1.0$, $ps>0.5$. In terms of RT variability, results did not yield reliable main effects for task or time, $Fs(1,6)=2.02$ and 0.08, $ps=0.20$ and 0.82; however, a task by time interaction, $F(1,6)=6.01$, $p=0.05$, demonstrated that antisaccade values decreased from baseline to post-intervention ($t(6)=2.56$, $p=0.04$), whereas prosaccade values did not reliably differ between time points ($t(6)=0.79$, $p=0.46$) (Figure 2).

RT skewness did not reveal reliable main effects or interactions (all $F < 1.83$, $ps > 0.22$); that is, the distribution symmetry for baseline pro- (0.95,

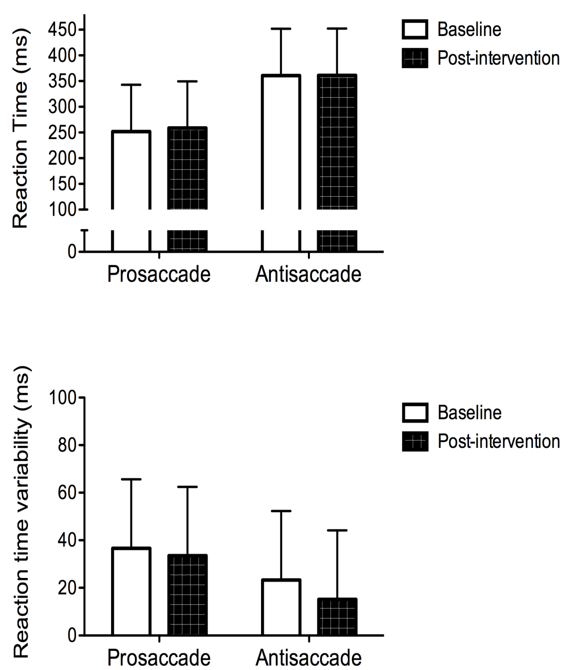


**Figure 2**: Mean reaction time (ms: top panel) and reaction time variability (ms: bottom panel) for pro- and antisaccades completed at baseline and post-intervention time points. Error bars represent 95% within-participant confidence intervals.

SD=1.01) and antisaccades (0.64, SD=0.56) did not reliably differ from their post-intervention counterparts (prosaccade: 0.85, SD=1.02; antisaccade: 0.34, SD=0.77).

Two-tailed Pearson's correlations were run to examine baseline and post-intervention pro- and antisaccade RTs with a cognitive assessment via the MoCA (assessed at baseline). Baseline and post-intervention prosaccade RTs, as well baseline antisaccade RTs, did not reliably relate to MoCA scores (all r=0.24, 0.22, 0.26, ps>0.60). In turn, post-intervention antisaccade RTs and MoCA scores demonstrated a reliable relationship (r=-0.81, p=0.04), such that faster post-intervention antisaccade RTs were associated with higher MoCA scores.

## Discussion

To our knowledge, this is the first report examining whether a 12-week SSE cognitive training intervention improves executive-related oculomotor control in octogenarians with objective cognitive impairment. The main challenge associated with completing the oculomotor assessment in our cohort was eligibility. There were many participants in the larger RCT who were willing to participate; however, due to severe macular degeneration and/or glaucoma, many were excluded in this sub-study, resulting in a final sample of seven. The large number of prospective participants with eye disease precluding oculomotor assessment is perhaps not surprising because in Canada, approximately 5.5 million people have one of the four most common eye diseases (glaucoma, cataracts, diabetic retinopathy, and age-related macular degeneration). Further, it is estimated that 1.4 million Canadians have age-related macular degeneration, which is expected to increase 30% in the next 10 years, and 250,000 are living with glaucoma (CNIB, 2015; Millar, 2004). Therefore, it is not unreasonable that we had issues with eligibility in this sub-study. Future work in this area should first aim to achieve a larger sample population to understand average antisaccade RTs in octogenerians prior to further interventional investigation.

Our group has previously shown that adults with subjective and/or objective cognitive impairments show a large magnitude (i.e., 25-30 ms) improvement in antisaccade RTs following a six-month aerobic or multi-modality exercise program (Heath et al., 2017, 2016). These improvements were shown to be maintained up to six months after the intervention ended (Shellington et al., 2017). Notably, however, that work showed that prosaccade RTs were not modified via an exercise intervention – a finding demonstrating that exercise produces an executive-specific improvement to executive control. Thus, our previous results provide a framework to demonstrate that executive-related improvements are due to a long duration moderate intensity exercise program (Heath et al., 2017, 2016).

Our group's previous work involved adults who were younger (mean ages 65-72 years), with interventions that were three times per week for 24-weeks at a moderate-intensity with or without dual-task (i.e., aerobic exercise combined with cognitive challenging questions) or SSE training (Heath et al., 2017, 2016). In contrast, our current exploratory intervention was only twice per week for 12-weeks of cognitive training and did not show a post-intervention reduction in antisaccade RTs or a modification in the symmetry of antisaccade distributions.

That said, we did observe decreased variability in antisaccade RTs – but not prosaccades – from baseline to post-intervention and we believe that this result provides some evidence of improved stability in evoking the appropriate executive demanding response plan for an antisaccade.

As mentioned above, we did not observe a post-intervention improvement in antisaccade RTs. At the outset, such a result suggests that a 12-week cognitive training program may not benefit brain health in octogenarians living in RL homes. Thus, it may be that our intervention was not of sufficient duration and/or did not include sufficient training sessions per week. In support of this view, there is some evidence that interventions to improve cognition should last at least six-months (Young et al., 2015). Unfortunately, we were unable to commit to a longer-term intervention because of time constraints and the frailty of the participants enrolled in our study. It is equally important to recognize that antisaccade RTs did not deteriorate over the duration of our intervention; that is, we did not observe a continued executive decline. The fact that antisaccade RTs did not decline provides partial evidence that our SSE intervention supported maintenance of executive control and therefore represents a positive outcome in this elderly population with objective cognitive impairment. Previous reports have shown that a lack of exercise participation (i.e., control group) in adults aged 68.7 (SD 8.5) with subjective or objective cognitive impairment is associated with a decline in cognition over 24-weeks (Lautenschlager, et al., 2008). Additionally, our previous work, which demonstrated improvements, was moderate-intensity exercise (Heath et al., 2017, 2016) and it is thought that aerobic exercise increases cerebral blood flow to improve structure and function (Voss et al., 2014). In contrast, SSE on its own may be too low of an intensity to elicit neuroprotective benefits but may provide a sufficient environment to maintain executive function in an elderly population with objective cognitive impairment. Of course, we recognize that because we did not use a control group it is not possible to definitively state that our intervention lead to the maintenance of executive-related oculomotor control in octogenarians; however, we feel that our results add importantly to the literature insomuch as they demonstrate that our intervention may serve to promote brain health.

### *Limitations*

One major limitation was a lack of a control group in this investigation; antisaccade RT was a tertiary outcome of a larger RCT and thus, this was an exploratory study. Additionally, it was difficult to recruit eligible participants and follow them up for 6 months due to deteriorating eye-health. Accordingly, we viewed the present work as an exploratory investigation in a population that has not been previously studied to assess feasibility. A second major limitation was the small sample size, and therefore our results should be interpreted with caution. Further, a repeated study that is powered for antisaccade RT should be conducted.

### *Conclusions*

Our results demonstrated that antisaccade RT assessed via video-based eye-tracking in octogenarians had limited feasibility due to age-related eye disease. We showed maintenance of executive-related oculomotor control in octogenarians with objective cognitive impairment over a 6-month period, including a 12-week cognitive training program. We cannot conclude that the maintenance was due to the 12-week SSE program because of the lack of control group and small sample size. However, this novel application of antisaccade RT adds to our understanding of executive-related oculomotor control in elderly adults and how they respond over a six-month period.

## Acknowledgements

Funding for this project was provided by the Department of Family Medicine, University of Western Ontario, Schlegel-University of Waterloo Research Institute for Aging, Ontario Graduate Scholarship (Author EMS), and Canadian Frailty Network Summer Student Award (Author AP). The Natural Sciences and Engineering Research Council of Canada (NSERC) provided funding support for the purchase of the eye-tracker and software development. We would like to thank the Residents of the Village of Winston Park and acknowledge the Schlegel Village staff, volunteers and students who championed this project for us: Tonya Bowles, Raymond Bolton, Emma Bender, Pamela Helmes-Hayes.

## Author Qualifications

The authors' qualifications are as follows: Erin M. Shellington PhD, MSc; Matthew Heath, PhD; Andrea F.M. Petrella MSc; Dawn P. Gill PhD; and Robert J. Petrella MD, PhD.

## References

Brown, A. K., Liu-Ambrose, T., Tate, R., and Lord, S. R. (2009). The effect of group-based exercise on cognitive performance and mood in seniors residing in intermediate care and self-care retirement facilities: a randomised controlled trial. *British journal of sports medicine*, *43*(8), 608–614.

Canadian Institute for Health Information (CIHI). (2011). Health Care in Canada , 2011 A Focus on Seniors and Aging. *Cihi*, 162. Retrieved from https://secure.cihi.ca/free_products/HCIC_2011_seniors_report_en.pdf

CNIB. (2015). Fast Facts. *Media and Publications*. Retrieved January 16, 2018, from http://www.cnib.ca/en/about/Publications/Pages/Fast-Facts.aspx#aboutLoss

Colcombe, S. J., Kramer, A. F., Erickson, K. I., Scalf, P., McAuley, E., Cohen, N. J., Webb, A., Jerome, G.J., Marquex, D.X., and Elavsky S.. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences*, *101*(9), 3316–3321. http://www.pnas.org/cgi/doi/10.1073/pnas.0400266101

Erickson, K. I., Voss, M. W., Prakash, R. S., Basak, C., Szabo, A., Chaddock, L., Kim, J. S., Heo, S., Alves, H., White, S.M., Wojcicki, T.R., Mailey, E., Vieira, V.J., Martin, S.A., Pence, B.D., Woods, J.A., McAuley, E., and Kramer. A.F.. (2011). Exercise training increases size of hippocampus and improves memory. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(7), 3017–22. http://www.pnas.org/content/108/7/3017

Everling, S., and Johnston, K. (2013). Control of the superior colliculus by the lateral prefrontal cortex. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*, *368*(September), 20130068. doi: 10.1098/rstb.2013.0068.

Gill, D. P., Gregory, M. A., Zou, G., Liu-Ambrose, T., Shigematsu, R., Hachinski, V., Fitzgerald, C., and Petrella., R.J.. (2016). The healthy mind, healthy mobility trial: A novel exercise program for older adults. *Medicine and Science in Sports and Exercise*, *48*(2), 297–306. doi: 10.1249/MSS.0000000000000758.

Heath, M., Shellington, E. M., Gill, D. P., and Petrella, R. J. (2017). A 24-week multi-modality exercise program improves executive control in older adults with a self-reported cognitive complaint: evidence from the antisaccade task. *Journal of Alzheimer's Disease*, *56*(1), 167–183. doi: 10.3233/JAD-160627.

Heath, M., Weiler, J., Gregory, M. A., Gill, D. P., and

Petrella, R. J. (2016). A Six-Month Cognitive-Motor and Aerobic Exercise Program Improves Executive Function in Persons with an Objective Cognitive Impairment: A Pilot Investigation Using the Antisaccade Task. *Journal of Alzheimer's Disease*, *54*(3), 923–931.

Lautenschlager, N. T., Cox, K. L., Flicker, L., Foster, J. K., and Bockxmeer, F. M. Van. (2008). Effect of Physical Activity on Cognitive Function in Older Adults at Risk for Alzheimer Disease. *Journal of American Medical Association*, *300*(9), 1027–1037. doi: 10.1001/jama.300.9.1027.

Liu-Ambrose, T., Nagamatsu, L. S., Graf, P., Beattie, B. L., Ashe, M. C., and Handy, T. C. (2012). Resistance Training and Executive Functions: A 12-Month Randomised Controlled Trial. *Arch Intern Med*, *170*(2), 170–178. doi: 10.1001/archinternmed.2009.494.

Millar, W. J. (2004). Vision problems among seniors. *Statistics Canada Catalogue: Health Reports*, *16*(1), 45–49. http://www.ncbi.nlm.nih.gov/pubmed/15581134

Munoz, D. P., Broughton, J. R., Goldring, J. E., and Armstrong, I. T. (1998). Age-related performance of human subjects on saccadic eye movement tasks. *Experimental Brain Research*, *121*(4), 391–400.

Munoz, D. P., and Everling, S. (2004). Look away: the anti-saccade task and the voluntary control of eye movement. *Nature reviews. Neuroscience*, *5*(February), 218–228.

Nagamatsu, L., Chan, A., Davis, J. C., Beattie, B. L., Graf, P., Voss, M. W., Sharma, D., and Liu-Ambrose, T.. (2013). The effects of exercise on memory performance in older adults with probable mild cognitive impairment: A 6-month randomized controlled trial. *Alzheimer's & Dementia*, *9*(4, Supplement), 293–294.

Peltsch, A., Hemraj, A., Garcia, A., and Munoz, D. P. (2014). Saccade deficits in amnestic mild cognitive impairment resemble mild Alzheimer's disease. *The European journal of neuroscience*, *39*(11), 2000–13. doi: 10.1111/ejn.12617.Shellington, E. M., Heath, M., Gill, D. P., and Petrella, R. J. (2017). Long-term maintenance of executive-related oculomotor improvements in older adults with self-reported cognitive complaints following a 24-week multiple modality exercise program. *Journal of Alzheimer's Disease*, *58*(1), 17–22. doi: 10.3233/JAD-161190.

Sperling, R. A., Aisen, P. S., Beckett, L. A., Bennett, D. A., Craft, S., Fagan, A. M., Iwatsubo, T., Jack, C.R. Jr, Kaye, J., Montine, T.J., Reiman, E.M., Rowe, C.C., Siemers, E., Stern, Y., Yaffe, K., Carrillo, M.C., Thies, B., Morrison-Bogorad, M., Wagster, M.V., and Phelps, C.H.. (2011). Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging- Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's Dement.*, *7*(3), 280–292. doi: 10.1016/j.jalz.2011.03.003.

Teixeira, C. V. L., Gobbi, S., Pereira, J. R., Vital, T. M., Hernandéz, S. S. S., Shigematsu, R., and Gobbi, L. T. B. (2013). Effects of square-stepping exercise on cognitive functions of older people. *Psychogeriatrics*, *13*(3), 148–156.

Voss, M. W., Erickson, K. I., Prakash, R. S., Chaddock, L., Kim, J., Alves, H., Szabo, A., White, S., Wojcicki, T.R., Mailey, E., Olson, E.A., Gothe, N.P., Potter, V.V, Martin, S.A., Pence, B.D., Cook, M.D., WOods, J.A., McAuley, E., and Kramer, A.F.. (2014). Neurobiological markers of exercise-related brain plasticity in older adults. *Brain Behaviour Immun.*, *28*(319), 90–99. doi: 10.1016/j.bbi.2012.10.021. E

Young, J., Angevaren, M., Rusted, J., and Tabet, N. (2015). Aerobic exercise to improve cognitive function in older people without known cognitive impairment. *Cochrane Database of Systematic Reviews*, (4). Retrieved from http://doi.wiley.com/10.1002/14651858.CD005381.pub4