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Eastern Kentucky University

The Effects of Cognitive Training on Neurodegenerative Disease: A Proposed Study

Honors Thesis

Submitted

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By

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The Effects of Cognitive Training on Neurodegenerative Disease

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Alzheimer's Disease (AD) and other neurodegenerative diseases impact over 5 million Americans and costs over \$290 billion annually. One possible method to restore cognitive functioning is cognitive training. Cognitive training is a broad term and can include activities like brain games, puzzles, meditation, music training, and many more activities. While there have been many studies researching individual forms of cognitive training, none have researched combining two forms of training. This research will study the effects of a combined cognitive training programming that includes 1) music training and 2) exergaming. Exergaming is a new form of training combining aerobic exercise and cognitive training on participants with AD. Other research has found positive effects of these training programs separately; therefore, it is reasonable to conclude that they will have at least a positive, non-interactive effect on cognitive functioning.

Keywords: Alzheimer's disease, cognitive training, exergaming, musical training

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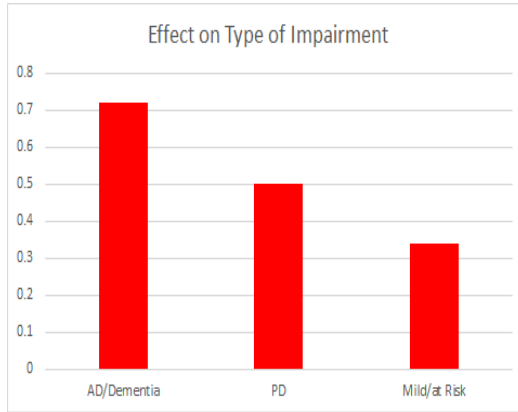


Figure 2: Musical history questionnaire that will be given to each participant.

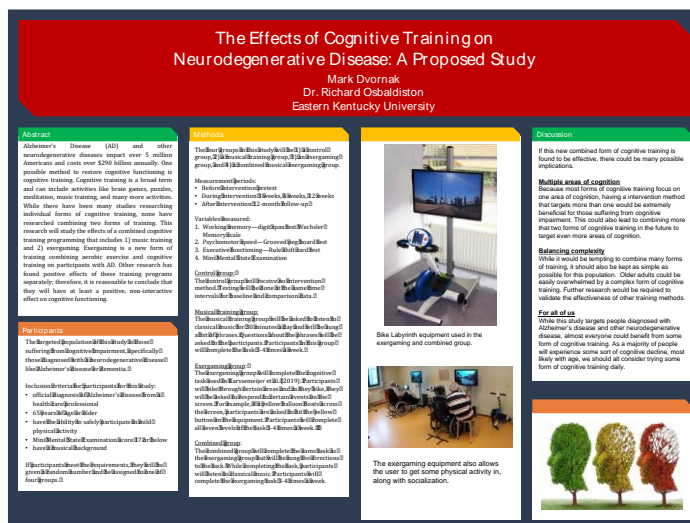
Musical History Questionnaire

Participant's Name: _____

Please circle your answers below.

- Have you ever been trained to play a musical instrument or sing?
 - Yes.
 - No
- If you answered Yes to question 1: How long have you played this instrument or sang?
 - Less than 5 years.
 - 5 years or more.
- Do you have the ability to read notes?
 - Yes.
 - No.

Figure 3: Poster submitted to MAUPRC



Acknowledgements

I would like to thank Dr. Richard Osbaldiston for his help and expert guidance throughout the completion of this project. His knowledge on statistical analysis and experimental design was crucial in creating a well-rounded and thorough proposal. I would also like to thank the Honor's program for giving me the opportunity to complete this thesis project and share my research on something that I am truly passionate about. Additionally, I would like to thank Madison Major and Jackson O'Daniel for their work on the meta-analysis that this proposal was founded on.

Introduction

As a person ages, it is normal for them to experience cognitive decline. This has led researchers to find ways to combat this decline in cognitive functionality. While effective methods have been found, millions of people are not as fortunate to experience this cognitive decline naturally and are diagnosed with a neurodegenerative disease. Neurodegenerative diseases such as Alzheimer's disease, dementia, Parkinson's disease, and many more have a drastic and rapid impact on an individual's cognitive functionality. A person diagnosed with Alzheimer's disease (AD) might experience a loss in language ability, memory, reasoning and an inability to take care of themselves and it is estimated that 5.8 million Americans are diagnosed with this disease and it costs over \$290 billion yearly (Alzheimer's Association, 2019). Currently, there is no cure for a neurodegenerative disease and many, if diagnosed, are fatal. With there being such a large population diagnosed with neurodegenerative diseases and there being no cure, many have researched possible ways to slow the neurodegeneration associated with these diseases and give the people diagnosed with it some cognitive function back. One suggested method to restore cognitive functioning within this population is cognitive training. Cognitive training is a very broad term and can include activities like brain

games, puzzles, meditation, music training, and many more. Cognitive training has found success in older populations of people who report having memory problems. Pereira-Morales, Cruz-Salinas, Aponte, and Pereira-Manrique (2018) researched the benefits of a computerized cognitive training method on participants who were not happy with their memory. They developed a web-based program that targeted many different aspects of cognition, such as attention, short- and long-term memory, orientation, and executive functioning. After implanting this form of training on twelve individuals in the computerized training group for eight weeks, researchers found a significant increase in the participants' cognition and short-term memory (Pereira-Morales, Cruz-Salinas, Aponte & Pereira-Manrique, 2018). The results from this study show that cognitive training can be used as an effective, non-pharmacological method for increasing cognitive functioning in populations that struggle with cognitive decline, such as people diagnosed with neurodegenerative diseases like Alzheimer's disease and dementia. Not only does cognitive training have promising results, but many forms of cognitive training do not require a professional to implement them or continue doing them, many can be done by the average person in the comfort of their own home.

Prior Research

Researching AD has always been an interest of mine as I have personally seen the drastic neurodegeneration caused by the disease. This experience had great impact on my decision to research and conduct a meta-analysis on a similar topic in the Spring of 2019. For this research my team, which consisted of Madison Major and Jackson O'Daniel and were mentored by Dr. Richard Osbaldiston, were all interested in cognition and how this new method of training could possibly be used to prevent the cognitive decline associated

with many forms of neurodegenerative diseases. This research consisted of looking at a multitude of cognitive training methods and many forms of neurodegenerative diseases. While the meta-analysis found that cognitive training did have a significant impact on cognitive functionality with this population, it left me with even more questions to research. One comment that my team and I got when presenting this research was the scope of the research. Many professionals thought that this was good initial research but lacked specifics. Since this was such a popular and polarizing topic to research, they wanted to know more. What cognitive training method worked the best? What population is this cognitive training most effective on? What does this mean for future research? These questions and comments sparked my interest in continuing and expanding upon this research for my honors thesis.

When starting this project, one adjustment I wanted to make was only looking at one neurodegenerative disease. Since my team had received feedback that our original study's scope was too large, I wanted to focus this research on the group that would most likely benefit the most from cognitive training. When collecting data for our original meta-analysis, our team focused on three different forms of neurodegeneration: AD and dementia, Parkinson's disease, and mild cognitive impairment. After collecting over 30 studies that focused in this area of research, my team narrowed it down to 15 studies. A graph depicting our results can be seen in Figure 1. Results from this meta-analysis found that people diagnosed with AD and dementia were affected the most ($d = 0.72$) followed by Parkinson's disease ($d = 0.50$) and those suffering from mild cognitive impairment were affected the least ($d = 0.34$). Due to the results from my previous research, I decided

to focus on those diagnosed with AD.

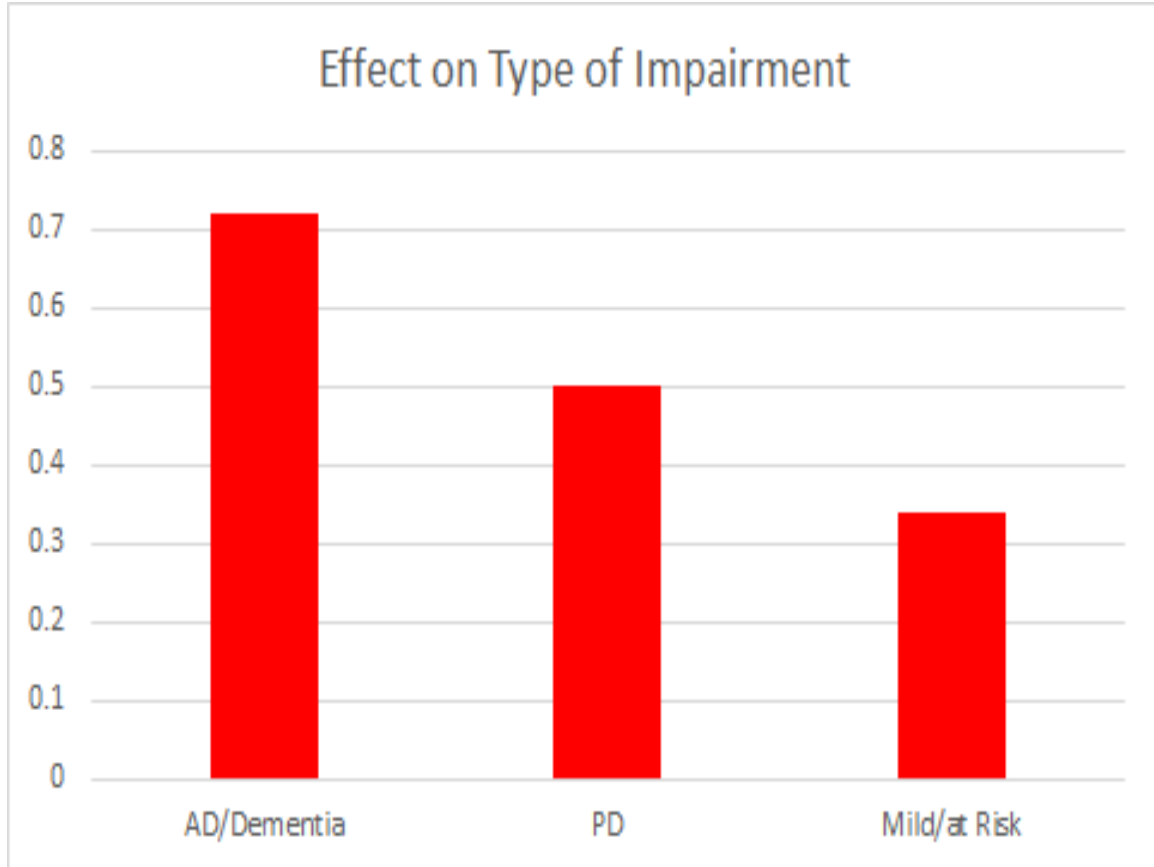


Figure 1: Meta-analysis data. Y-axis represents the Cohen's d value.

While completing initial research for this thesis, I noticed a problem and gap in the research available on cognitive training. While there are many different forms of cognitive training, some only target certain areas of cognitive functioning. For example, if someone was diagnosed with AD and starting using an exergaming form of cognitive training, they might only see an increase in cognitive functioning in psychomotor speeds (Karssemeijer, Aaronson, Bossers, Donders, Olde Rikkert, & Kessels, 2019). While it would be beneficial for this population to have this increase in psychomotor speeds, there are still many different areas of cognitive functioning that are not improved. Other areas, like memory, are addressed in different forms of cognitive training. Innes et al. (2018)

implemented both musical and meditation based cognitive training on individuals with cognitive decline and found a significant increase in subjective memory functioning. While it would be beneficial for someone suffering from cognitive decline or a neurodegenerative disease to participate in any form of cognitive training that would increase one aspect of cognitive functioning, would it not be more beneficial for them to participate in a training method that targets and affects more than one area? This question inspired me and led me to my current thesis project. Creating a new combined form of cognitive training that could be used to target multiple areas of cognitive functioning. Creation of this new form of cognitive training will be done by writing a research proposal for a study that can be completed in the future.

Proposal

Cognitive Training

The first step in writing this proposal and creating this study was finding the two forms of cognitive training that I wanted to combine. The first method of cognitive training that I decided to use in this study was exergaming. Exergaming combines physical aerobic activity with a cognitive task. In 2019, Karssemeijer et al. researched the impact of exergaming on cognitive functionality on those diagnosed with dementia. 115 people were allowed to participate in this study and were broken up into three different groups: exergaming, aerobic exercise, and a control group. The control group only did mild relaxation and flexibility training and the aerobic exercise group rode a stationary bicycle for 30 minutes at a time. The exergaming group rode a special bicycle designed by Bike Labyrinth (www.bikelabyrinth.com). This bicycle is connected to a monitor and as the participant rides through different areas across the world, they will complete

cognitive tasks. For example, as a participant is riding down the streets of New York City, they might see a yellow balloon float across the screen. Before starting the session, participants would be told to press the yellow button on their bicycle when they see this. There are multiple levels to the exergaming activity and as the participant moves through the levels, they will increase in difficulty. For example, balloons floating across the screen show up for a shorter amount of time or a hot air balloon matching the same color might float across the screen, which they had been told to ignore (Karssemeijer, Bossers, Aaronson, Kessels & Olde Rikkert, 2017). Each group would complete their training three times a week for twelve weeks. While it was originally hypothesized that the exergaming group would see an increase in executive functioning, researchers found that there was a significant increase in psychomotor speeds with a moderate effect size (.102) (Karssemeijer et al., 2019). Due to the results of this study, it is likely to hypothesize that combining exergaming with another form of cognitive training will result in a significant increase in psychomotor speeds.

If the new form of cognitive training involving exergaming does not have a significant impact on the participants, it will still be beneficial to participate in. Exercise is known to be extremely beneficial for those diagnosed with AD and other neurodegenerative diseases as it can improve neuroplasticity, the immune system, and increase hippocampal functioning (Intlekofer & Cotman, 2013).

The cognitive training method that will be combined with exergaming will be music training. Musical forms of cognitive training can take many forms, for this study two different forms will be used. The first form of music training is music listening. Researchers found that by simply listening to classical music for at least 12 minutes a day

for three months improved participant's memory with subjective cognitive decline (Kandati, Innes, Selfe & Khalsa, 2017). This study took place over six months and after the first three months of the intervention, participants were told that it was not mandatory to complete every day. At the six-month testing time, participants maintained the progress made in the first three months or saw improvements in memory (Kandati, Innes, Selfe & Khalsa, 2017). The second form of musical training that will be used is musical mnemonics training. Baird, Samson, Miller, and Chalmers (2017) studied the impact that musical mnemonics can have on verbal memory in participants with AD. Additionally, in this study they researched the impact of having a musical background and how that effects the efficiency of musical mnemonics. In their study, participants were broken up into two different groups: spoken and sung. In the spoken group, participants were spoken phrases that they would be asked about later. In the sung group, the same phrases were sung to the participants to a familiar Australian song. After five trials, results from the study indicated that musicians with AD were able to learn the sung information better than those without a musical background (Baird, Samson, Miller & Chalmers, 2017). Given the findings of these studies, it is reasonable to conclude that the same effect will be seen when combined with another form of cognitive training.

Participants

Since this study will be involving human participants, approval will be needed from the Institutional Review Board. Since prior research revealed that people diagnosed with AD would benefit the most from cognitive training, I knew that I wanted to focus on those diagnosed with AD in hopes of restoring cognitive functionality. According to the Mayo Clinic (2020), the majority of diagnosis for AD happen in the age range of 65 to

74. Additionally, early-onset AD is defined as being diagnosed with AD before the age of 65 and is most likely caused by genetic mutations (Mendez, 2019). To avoid mixing these two populations of people with AD, there is a requirement for a diagnosis at or after the age of 65. Participants must also take the Mini-Mental State Examination (MMSE) and receive a score of 17 or less. The MMSE is the most used examination that evaluates cognitive impairment and is commonly used to assess those with cognitive impairment in a research setting (Arevalo-Rodriguez et al., 2015). Having each participant take this before starting the new combined form of cognitive training will ensure that all participants are at similar levels of cognitive impairment. Since some of the participants would be engaging in physical activity, they need to have a physical conducted on them within the last six months and they need to be able to safely operate the exergaming equipment. Additionally, the participants need to have a musical background in order to participate in this study. Research indicates that the musical mnemonics training will be the most effective on those with a musical background (Baird, Samson, Miller & Chalmers, 2017). To determine whether or not a participant has a musical background, I created a musical background questionnaire for each participant to complete. To have a musical background, participants must have played a musical instrument for 5 or more years of their life and be able to read musical notes.

Musical History Questionnaire

Participant's Name: _____

Please circle your answers below.

1. Have you ever been trained to play a musical instrument or sing?
a. Yes. b. No
2. If you answered Yes to question 1: How long have you played this instrument or sang?
a. Less than 5 years. b. 5 years or more.
3. Do you have the ability to read notes?
a. Yes. b. No.

Figure 2: Musical history questionnaire that will be given to participants.

If the participants meet the aforementioned requirements, they will be assigned a number and using random assignment will put into one of four groups: a control, musical training, exergaming, and combined musical exergaming.

Measurements

This study will have four dependent variables that will be measured before the intervention starts, at 3 weeks, at 6 weeks, at 12 weeks, and an optional testing 12 months after the study has concluded. The optional testing 12 months after the intervention has concluded is to test the long-term effect of the cognitive training.

The four dependent variables are the MMSE, working memory, executive functioning, and psychomotor speed. While the MMSE does not give an in-depth look at a specific area of cognitive functionality, it does give information about the level of cognitive impairment that the participant is at. This will be valuable information as it will give insight how improvements in individual areas of cognition affect the level of cognitive impairment.

Working memory will be measured using the digit span test from the Wechsler Memory Scale. For this test, participants will be read a series of numbers and will be asked to repeat the series back to the tester. Scoring of this test will be based off of the number of correct responses (Fink, Hemmy, MacDonald et al., 2014).

Executive functioning will be measured using the rule shift card test. This test uses 21 playing cards and a set of rules. The rules to this test will be shown to the participant at all times. The tester will flip through the 21 cards and will ask the participant to respond to the card based upon the rules. Scoring of this test will be the amount of time it takes a participant to make it through all 21 cards correctly and the number of errors made while going through the cards (Espinosa et al., 2009).

Psychomotor speeds will be measured using the grooved pegboard test. Participants will be given the pegboard and will be told to complete the test as quickly as possible. Scoring for this test will be based off of how long it takes the participant to complete the test (Schmidt, Oliveira, Rocha & Abreu-Villaça, 2000).

Experimental Groups

The control group in this study will receive no intervention method. Participants assigned to this group will take the same tests as the other groups at the same time. Data

from this group will be used as baseline and comparison data so that a two-way ANOVA statistical analysis can be used to calculate the effect size of the different cognitive training methods.

The musical training group will have two different tasks to complete. The first task will be music listening. Participants in this group will be told to listen to at least 15 minutes of classical music a day. Participants will be given a playlist of music that they can choose from to listen to. The second task will be similar to Baird et al. (2017), where the participant will be sung phrases and asked questions about them after. Participants are required to complete both tasks four times a week. This group will be tested before the intervention starts, at 3 weeks, 6 weeks, 12 weeks, and an optional testing 12 months after the intervention has concluded.

The exergaming group will complete the same cognitive task described in Karssemeijer et al. (2017) and used in Karssemeijer et al. (2019). Participants will use the Bike Labyrinth equipment for at least 30-45 minutes or one riding session four times a week. Before starting each session, the rules of the task will be reminded to participant. This group will be tested before the intervention starts, at 3 weeks, 6 weeks, 12 weeks, and an optional testing 12 months after the intervention has concluded.

The combined group will be a combination of the exergaming and musical training groups. Participants in this group will complete the same task as the exergaming group, using the Bike Labyrinth equipment for 30-45 minutes or one riding session four times a week. To help with memory of the rules of the task, a prerecorded song will be played for the participant describing the rules of the task and what the participant should be doing while riding. This will only be played once per riding session but before every

session begins. While the participant is completing the exergaming task, a compilation of classical music will be played for the participant for the entirety of the session. This group will be tested before the intervention starts, at 3 weeks, 6 weeks, 12 weeks, and an optional testing 12 months after the intervention has concluded.

Discussion

While working on this proposal this semester, I was encouraged by Dr. Osbaldiston to submit my proposal to many different conferences around the state of Kentucky. Attending these conferences would be a way to for me to share my research and proposal within the field. Not only would I be sharing it, but this would also be a valuable source of feedback from experienced members in the community.

Unfortunately, due to the COVID-19 global pandemic, all conferences in the foreseeable have been cancelled. Although all in-person conferences have been cancelled, some conferences have been moved to online. The Mid-American Undergraduate Psychology Research Conference (MAUPRC) is taking place on April 24th, 2020 and I have submitted a poster to present. The poster (Figure 2) outlines the most essential parts of the study by giving the reader the rationale behind the research, population and

participants, the experimental tasks, measurements, and a discussion section.



Figure 3: Poster submitted to MAUPRC

While Alzheimer's disease is a heavily researched topic, researchers are just scratching the surface with their knowledge on the disease and other neurodegenerative diseases. Since there is no cure to the disease, these cognitive training methods have grown in popularity as a way to restore some cognitive functionality. While this is just a proposal for a study, it is reasonable to conclude, from past findings on the individual training methods, that this new form of cognitive training will be successful. If this study is conducted and found effective, it opens the door for researching other combined forms of cognitive training. Additionally, it opens the door for combining more than two forms of cognitive training to get the most benefit out of a single training method. Although this study targets those suffering from extreme forms of cognitive impairment, everyone can

benefit from the results as a majority of the population will suffer from some form of cognitive impairment at some point in their life.

References

- Advocat J, Enticott J, Vandenberg B, Hassed C, Hester J, & Russell G. (2016). The effects of a mindfulness-based lifestyle program for adults with Parkinson's disease: a mixed methods, wait list controlled randomised control study. *BMC Neurology*, 16, 166. <https://doi-org.libproxy.eku.edu/10.1186/s12883-016-0685-1>
- Arevalo-Rodriguez, I., Smailagic, N., Figuls, M. R. I, Ciapponi, A., Sanchez-Perez, E., Giannakou, A., Pedraza, O. L., Cosp, X. B., & Cullum, S. (2015). Mini-Mental State Examination (MMSE) for the detection of Alzheimer's disease and other dementias in people with mild cognitive impairment (MCI). *BJPsych Advances*, 21(6), 362. <https://doi-org.libproxy.eku.edu/10.1192/apt.21.6.362>
- Alzheimer's Association. (2019) *Alzheimer's Facts and Figures Report*. <https://www.alz.org/alzheimers-dementia/facts-figures>
- Baird, A., Samson, S., Miller, L., & Chalmers, K. (2017). Does music training facilitate the mnemonic effect of song? An exploration of musicians and nonmusicians with and without Alzheimer's dementia. *Journal of Clinical & Experimental Neuropsychology*, 39(1), 9–21. <https://doi.org/10.1080/13803395.2016.1185093>
- Barban, F., Mancini, M., Cercignani, M., Adriano, F., Perri, R., Annicchiarico, R., Carlesimo, G. A., Ricci, C., Lombardi, M. G., Teodonno, V., Serra, L., Giulietti, G., Fadda, L., Federici, A., Caltagirone, C., & Bozzali, M. (2017). A Pilot Study on Brain Plasticity of Functional Connectivity Modulated by Cognitive Training in Mild Alzheimer's Disease and Mild Cognitive Impairment. *Brain Sciences* (2076-3425), 7(5), 50. <https://doi-org.libproxy.eku.edu/10.3390/brainsci7050050>

- Belleville S, Clément F, Mellah S, Gilbert B, Fontaine F, & Gauthier S. (2011). Training-related brain plasticity in subjects at risk of developing Alzheimer's disease. *Brain: A Journal of Neurology*, 134(6), 1623–1634. <https://doi-org.libproxy.eku.edu/brain/awr037>
- Cavallo, M., Zanalda, E., Johnston, H., Bonansea, A., & Angilletta, C. (2016). Cognitive Training in a Large Group of Patients Affected by Early-Stage Alzheimer's Disease can have Long-Lasting Effects: A Case-Control Study. *Brain Impairment*, 17(2), 182–192. <https://doi-org.libproxy.eku.edu/10.1017/BrImp.2016.2>
- De Luca R, Bramanti A, De Cola MC, Leonardi S, Torrisi M, Aragona B, Trifiletti A, Ferrara MD, Amante P, Casella C, Bramanti P, & Calabro RS. (2016). Cognitive training for patients with dementia living in a sicilian nursing home: a novel web-based approach. *Neurological Sciences*, 37(10), 1685–1691. <https://doi-org.libproxy.eku.edu/10.1007/s10072-016-2659-x>
- Espinosa, A., Alegret, M., Boada, M., Vinyes, G., Valero, S., Martinez-Lage, P., . . . Tarraga, L. (2009). Ecological assessment of executive functions in mild cognitive impairment and mild Alzheimer's disease. *Journal of the International Neuropsychological Society*, 15(5), 751–757. doi:10.1017/S135561770999035X
- Fink, H. A., Hemmy, L. S., MacDonald, R. et al. (2014) *Cognitive Outcome After Cardiovascular Procedures in Older Adults: A Systematic Review*. Agency for Healthcare Research and Quality.
- Giovagnoli AR, Manfredi V, Parente A, Schifano L, Oliveri S, & Avanzini G. (2017). Cognitive training in Alzheimer's disease: a controlled randomized

study. *Neurological Sciences*, 38(8), 1485–1493. <https://doi-org.libproxy.eku.edu/10.1007/s10072-017-3003-9>

Intlekofer, K. A., & Cotman, C. W. (2013). Exercise counteracts declining hippocampal function in aging and Alzheimer's disease. *Neurobiology of disease*, 57, 47-55.

Janssen, A., Boster, A., Lee, H., Patterson, B., & Prakash, R. S. (2015). The effects of video-game training on broad cognitive transfer in multiple sclerosis: A pilot randomized controlled trial. *Journal of Clinical & Experimental Neuropsychology*, 37(3), 285–302. <https://doi-org.libproxy.eku.edu/10.1080/13803395.2015.1009366>

Kandati, S., Innes, K. E., Selfe, T. K., & Khalsa, D. S. (2017). Meditation and Music Improve Memory and Cognitive Function in Adults with Subjective Cognitive Decline: A Pilot Randomized Controlled Trial. *Journal of Alzheimer's Disease*, 56(3), 899–916. <https://doi.org/10.3233/JAD-160867>

Karssemeijer, E. G. A., Aaronson, J. A., Bossers, W. J. R., Donders, R., Olde Rikkert, M. G. M., & Kessels, R. P. C. (2019). The quest for synergy between physical exercise and cognitive stimulation via exergaming in people with dementia: a randomized controlled trial. *Alzheimer's Research & Therapy*, 11(1), N.PAG. <https://doi.org/10.1186/s13195-018-0454-z>

Karssemeijer, E.G.A., Bossers, W.J.R., Aaronson, J.A., Kessels, R. P. C., & Olde Rikkert, M. G. M. (2017). The effect of an interactive cycling training on cognitive functioning in older adults with mild dementia: study protocol for a randomized controlled trial. *BMC Geriatr* 17, 73. <https://doi.org/10.1186/s12877-017-0464-x>

- Lalanne, J., Gallarda, T., & Piolino, P. (2015). “The Castle of Remembrance”: New insights from a cognitive training programme for autobiographical memory in Alzheimer’s disease. *Neuropsychological Rehabilitation*, 25(2), 254–282.
- Lawrence, B. J., Gasson, N., Johnson, A. R., Booth, L., & Loftus, A. M. (2018). Cognitive Training and Transcranial Direct Current Stimulation for Mild Cognitive Impairment in Parkinson’s Disease: A Randomized Controlled Trial. *Parkinson’s Disease* (20420080), 1–12. <https://doi-org.libproxy.eku.edu/10.1155/2018/4318475>
- Li BY, He NY, Qiao Y, Xu HM, Lu YZ, Cui PJ, Ling HW, Yan FH, Tang HD, & Chen SD. (2019). Computerized cognitive training for Chinese mild cognitive impairment patients: a neuropsychological and fMRI study. *Neuroimage. Clinical*, 22, 101691. <https://doi-org.libproxy.eku.edu/10.1016/j.nicl.2019.101691>
- Mayo Clinic. (2018, December 8). *Alzheimer’s disease*. <https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/symptoms-causes/syc-20350447>
- Mendez, M. F. (2019). Early-onset Alzheimer disease and its variants. *CONTINUUM: Lifelong Learning in Neurology*, 25(1), 34–51.
- Nousia, A., Siokas, V., Aretouli, E., Messinis, L., Aloizou, A.-M., Martzoukou, M., Karala, M., Koumpoulis, C., Nasios, G., & Dardiotis, E. (2018). Beneficial Effect of Multidomain Cognitive Training on the Neuropsychological Performance of Patients with Early-Stage Alzheimer’s Disease. *Neural Plasticity*, 1–9. <https://doi-org.libproxy.eku.edu/10.1155/2018/2845176>

- Orrell M, Yates L, Leung P, Kang S, Hoare Z, Whitaker C, Burns A, Knapp M, Leroi I, Moniz-Cook E, Pearson S, Simpson S, Spector A, Roberts S, Russell I, de Waal H, Woods RT, & Orgeta V. (2017). The impact of individual Cognitive Stimulation Therapy (iCST) on cognition, quality of life, caregiver health, and family relationships in dementia: a randomised controlled trial. *Plos Medicine*, 14(3), e1002269. <https://doi-org.libproxy.eku.edu/10.1371/journal.pmed.1002269>
- Pereira-Morales, A. J., Cruz-Salinas, A. F., Aponte, J., & Pereira-Manrique, F. (2018). Efficacy of a computer-based cognitive training program in older people with subjective memory complaints: a randomized study. *International Journal of Neuroscience*, 128(1), 1–9. <https://doi.org/10.1080/00207454.2017.1308930>
- Schmidt, S., Oliveira, R., Rocha, R., & Abreu-Villaça, Y. (2000). Influences of Handedness and Gender on the Grooved Pegboard Test. *Brain and Cognition*. 44. 445-454. 10.1006/brcg.1999.1204.
- Styliadis, C., Kartsidis, P., Paraskevopoulos, E., Ioannides, A. A., & Bamidis, P. D. (2015). Neuroplastic Effects of Combined Computerized Physical and Cognitive Training in Elderly Individuals at Risk for Dementia: An eLORETA Controlled Study on Resting States. *Neural Plasticity*, 2015, 1–12. <https://doi-org.libproxy.eku.edu/10.1155/2015/172192>
- Tsantali E, Economidis D, & Rigopoulou S. (2017). Testing the benefits of cognitive training vs. cognitive stimulation in mild Alzheimer’s disease: a randomised controlled trial. *Brain Impairment*, 18(2), 188–196. <https://doi-org.libproxy.eku.edu/10.1017/BrImp.2017>.