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Exploring the Relation Between Aerobic Exercise, BDNF and Alzheimer's Disease: A Research Protocol

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Abstract

Introduction: Alzheimer's Disease (AD) is a neurodegenerative disease that impacts the aging population by causing severe cognitive decline. Although there is no cure for AD, studies have shown that lifestyle changes may contribute to preventing AD. The purpose of this study is to investigate how regular exercise can influence a positive change in the cognitive decline that is associated with AD in rats, through a rise in BDNF levels.

Methods: The study would be performed through a series of procedures and tests. Rats would be surgically induced with AD and separated into groups exposed to different aerobic exercise regiments. Then, they would either complete a novel object recognition test, to assess behavioural components, or magnetic resonance imaging, to assess structural components. Finally, they would have their brains extracted to measure protein levels.

Results: The rats who would have been surgically induced with AD and exposed to regular exercise, are anticipated to have performed better on the novel object recognition test, than the rats surgically induced with AD, but not exposed to regular exercise. The rats who would have been surgically induced with AD and exposed to regular exercise, are anticipated to have shown greater gray matter and hippocampal volume on the magnetic resonance imaging, exhibit greater levels of BDNF, and show decreased levels of Aβ peptides and p-tau during the protein level measurement, than the rats induced with AD but not exposed to regular exercise.

Discussion: The study would anticipate finding that the increased release of BDNF that occurs through regular exercise, decreases Aβ peptide and p-tau levels. Through decreasing Aβ peptide and p-tau levels, BDNF can be used as a form of neuroprotection in slowing down the cognitive decline that is associated with AD.

Conclusion: The measures applied when researching ways in which the cognitive decline brought on by AD in rats can be reduced, could potentially be translated to further studying therapeutic treatments for AD in humans. These results could lead to similar preventative measures for other neurodegenerative diseases. Future directions may include informing the public of the importance that lifestyle changes may have on neurological health.

Keywords: Alzheimer's disease; BDNF; Aβ peptides; cognitive decline; exercise; hippocampus

Introduction

Alzheimer's disease (AD) is a progressive, age-related neurodegenerative disease, resulting in cognitive decline, impairment and memory loss, and is the leading cause of dementia in the elderly [1]. AD impacts an area of the brain known as the hippocampus, which is essential for memory and learning [1]. Although there are no definitive cures for AD, there are a number of preventative measures, one of which may be aerobic exercise. Studies have shown that exercise in animals can have beneficial effects on improving cognitive function [1]. Hence, aerobic exercise is said to aid in preventing neurodegeneration, which is facilitated through changing levels of brain derived neurotrophic factor (BDNF) [1].

BDNF is a protein in the family of neurotrophic growth factors and is extremely significant in regulating axonal and dendritic growth, while also playing a crucial role in neuroprotection and neuronal survival [1,2]. Mature BDNF has been shown to strengthen synapses, proving to be an important regulator of learning and memory processes [2]. Additionally, the presence of BDNF is believed to prevent neurodegeneration through changing levels of amyloid-β (Aβ) peptides and *phosphorylated* tau protein (p-tau) [3].

Although there are many pathological features associated with AD, an increased presence of Aβ peptides and p-tau can be identified as the most significant biomarkers [4]. Aβ peptides are responsible for being the primary component of extracellular aging plaques, known as amyloid plaques, while the hyperphosphorylated p-tau form aggregates, composing neurofibrillary tangles (NFTs) [1]. These amyloid plaques and NFTs can form within neurons, essentially destroying cell function in the hippocampal region by decreasing the number of neural cells and synapses. [5].

Not only are Aβ peptides and p-tau believed highly associated with cognitive decline, but they are also said to contribute to pathologic changes such as neuroinflammation, loss of hippocampal volume, brain atrophy and neurovascular dysfunction [3]. These pathologic features are said to be associated with severe cognitive decline, such as learning and memory impairment. Many of the pathologic changes said to be associated with Aβ peptides and p-tau, can be visually seen, and confirmed through magnetic resonance imaging (MRI) [6]. MRI is a form of neuroimaging in which brain structure, volume and matter can be visualized as well as identified [7]. By using neuroimaging resources, such as MRI's, one can compare and contrast the physical features, that are said to be found in the AD brain, to the physical features that are associated with a healthy brain.

This study anticipates that AD rats who would have participated in regular exercise would exhibit results, in terms of structure and behavior, that corresponds to better cognition compared to those AD rats who would not have participated in exercise. AD is incredibly prevalent within society and impacts individuals negatively through cognitive decline. As of today, there are no known cures for AD, which is why it is important to study different ways in which the symptoms of AD can be aided through lifestyle changes. Thus, the purpose of the study is to explore how aerobic exercise may be used as a therapeutic treatment for AD to improve the structural and behavioural losses, through the interaction between BDNF, Aβ peptide and p-tau in the hippocampus.

Methods

Rodent

In this study, 48 adult Wistar rats would be housed in spacious cages with free access to food and water [8]. All rats would be familiarized with the laboratory environment for 5 weeks before half would be randomly selected to undergo AD induction (Aβ, Aβ+1E and Aβ+6E; n=24) (Figure 1) [8]. AD induction would be achieved through an injection of Aβ peptide in the hippocampus, following the Fakhraei et al methodology [1]. Aβ peptide would be dissolved in 3% DMSO buffer solution and stored at -80℃. [1] Approximately one month later, the solution would be incubated to Aβ fibril form [1]. For surgery, rats would be anesthetized using Ketamine and Xylazine, and the head of the animals would be fixed, holes in the posterior position would have been made into the skull, and Aβ (1 µl per side) would have been injected into the lateral ventricles using a Hamilton syringe [1,4]. This surgical procedure would be repeated for the control groups (C, C+1E, C+6E; n=24) but rather than receiving an Aβ injection, they would have received a saline injection (Figure 1).

Aerobic Exercise

The 48 rats would randomly be divided into six groups: Aβ injection (Aβ) (n = 8), Aβ injection + 1 week of exercise (Aβ+1E) (n = 8), Aβ injection + 6 weeks of exercise (Aβ+6E) (n = 8), control (C) (n = 8), control + 1 week of exercise (C+1E) (n = 8), and control + 6 weeks of exercise (C+6E) (n = 8) (Figure 1). The treadmill exercise training protocol was adapted from Zhang et al [9]. 2 weeks post-surgery, the groups Aβ+6E and C+6E would be exposed to 6 weeks of regular moderate-intensity aerobic exercise (5 days/week), in which they would train on a treadmill, in 2-20 minute intervals, with a 10 minute break in between each interval, at varying speeds (Figure 2a) [9]. During the first 2 weeks of training, the Aβ+6E and C+6E groups would participate in a 1 hour training session, at a speed of 15 m / min on the treadmill [9]. During the 3rd and 4th week of training, the Aβ+6E and C+6E groups would participate in a 1 hour training session, at a speed of 20 m / min on the treadmill [9]. During the 5th and final week of training, the Aβ+6E and C+6E groups would participate in a 1 hour training session at a speed of 25 m / min on the treadmill [9]. Additionally, during the final week of training, the Aβ+1E and C+1E groups would be exposed to the treadmill, as the training group (Figure 2a) [9]. Rats would be returned to home cages once they finished the exercise each day.

Testing Preparation

After the aerobic exercise is complete, the six groups of rats would be further divided into three activity groups (Figure 1). Three rats from each of the six groups would undergo an MRI, followed by brain extractions (MRI group; n= 18). Another three rats from each of the six groups would be taken to perform NOR tests, followed by brain extractions (NOR group; n=18). The final two rats from each of the six groups would be used as a control group and would participate only in brain extraction, to record measurements (NA group; n=12) (Figure 1).

Novel Object Recognition (NOR) Test

The NOR test is used to assess memory through novel and familiar object recognition [7]. The NOR test would be done following the Wan et al methodology, one day after the aerobic exercise was complete [10]. The test would be taken over the course of 3 days [9]. On day 1, the rats would be habituated to the testing box, freely exploring the empty box for 10 minutes [9]. On day 2, the rats would be placed in the same box and introduced to the 2 new identical objects that were placed at an equal distance away from the rats [9]. The rats would then be given 5 minutes to explore the box, alongside the 2 identical objects [9]. On day 3, the rats would be returned to the box that contained 1 of the objects from day 2, alongside a novel object that was different in shape and colour [9]. The rats would then be given 5 minutes to explore the box and objects [10]. The object would have been identified as explored once the rat's nose was pointed within 2 cm from the object [9]. Rats would then be returned to home cages once finished the NOR task each day. Recognition memory would have been measured with the time spent exploring a novel object and the time spent exploring a familiar object (Figure 2b) [9].

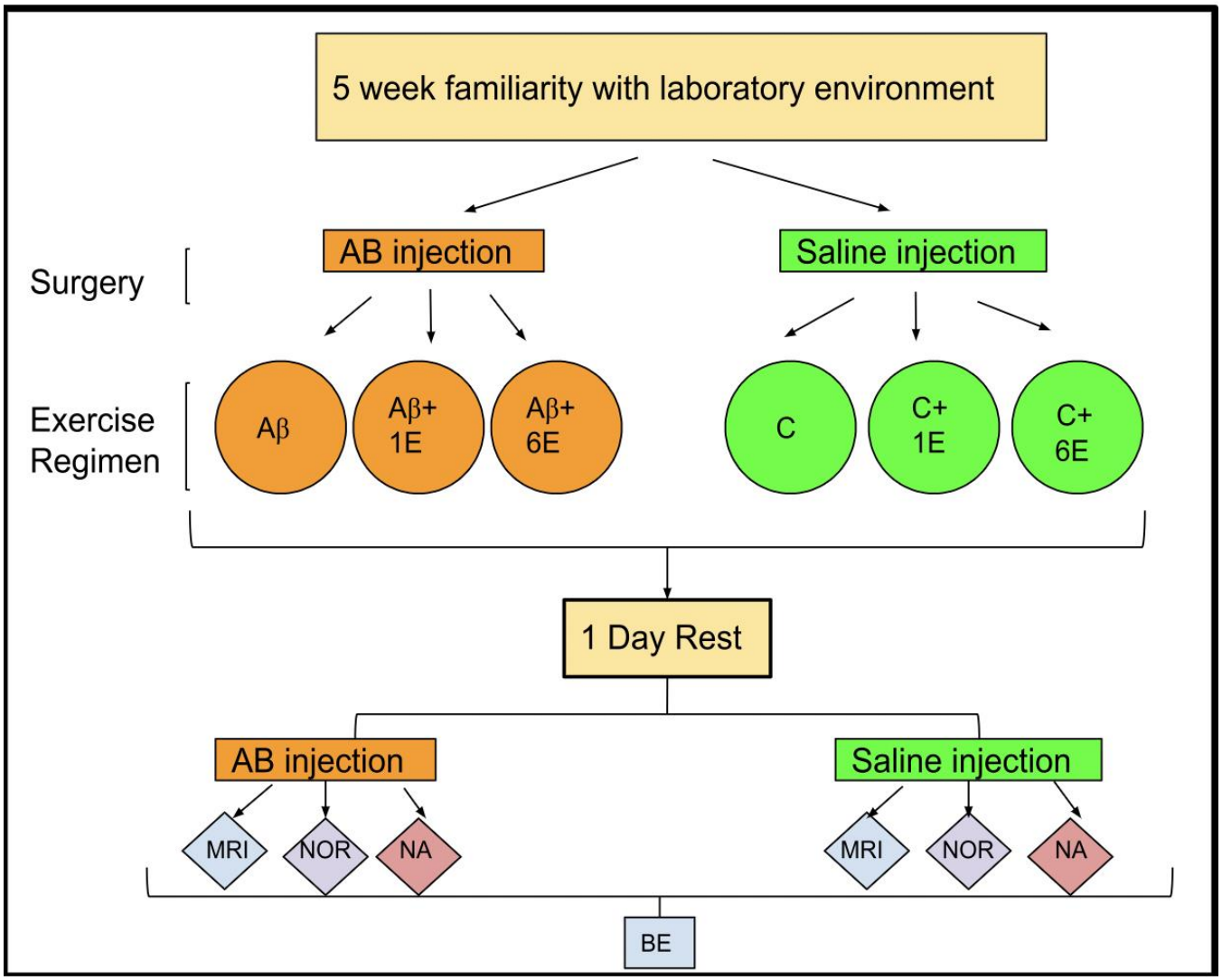
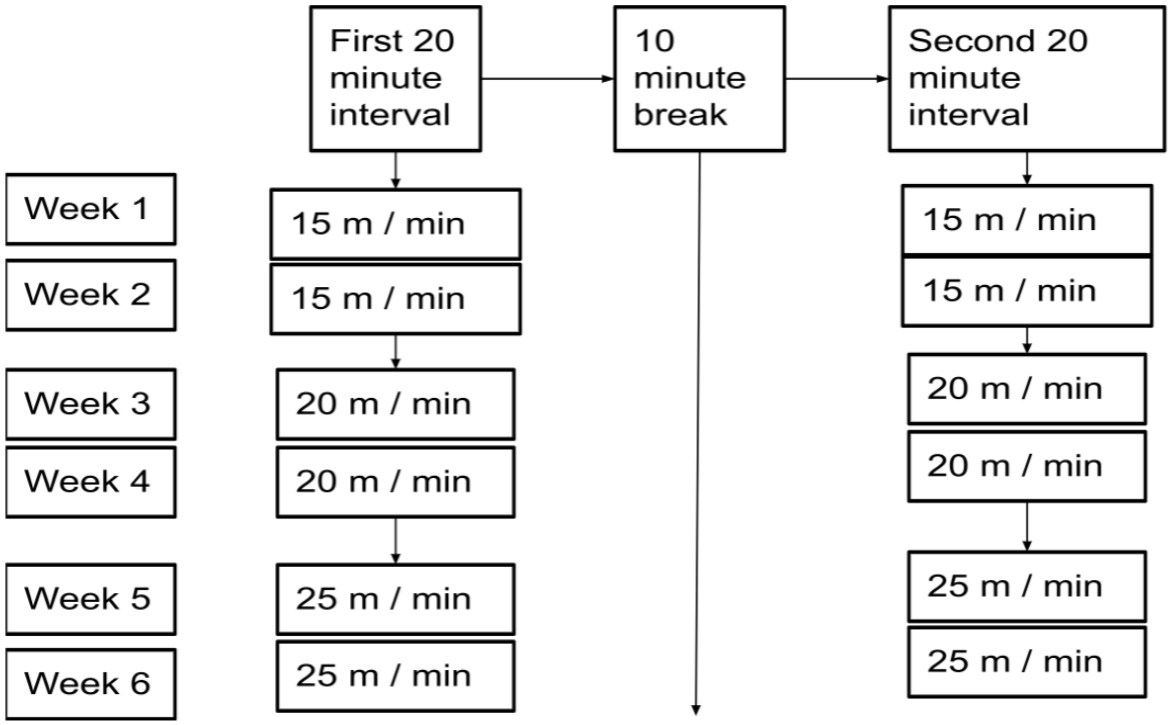


Figure 1. The study protocol timeline. The study starts off with the introduction of the 48 Wistar Rats to the laboratory environment, over the span of 5 weeks. Following this period, half the rats would be injected with Aβ, while the other half would be injected with saline. 2 weeks later, the rats would go through different aerobic exercise regimens. Group Aβ are rats who would have been injected with Aβ and would not participate in the exercise regimen at all. Group Aβ+1E are rats who would have been injected with Aβ and would only participate in the last week of the exercise regimen. Group Aβ+6E are rats who would have been injected with Aβ and would participate in all 6 weeks of the exercise regimen. Group C are rats who would have been injected with saline and would not participate in the exercise regimen at all. Group C+1E are rats who would have been injected with saline and would only participate in the last week of the exercise regimen. Group C+6E are rats who would have been injected with saline and participate in all 6 weeks of the exercise regimen. A day after the exercise regimen, all of the rats would be divided back into their injection groups and be further divided into three experimental groups - MRI (18 rats), NOR (18 rats) and no activity (NA, 12 rats) groups. In the MRI group, rats would be taken to get an MRI scan and then get their brain extracted. In the NOR group, rats would be taken to perform a NOR test and then get their brain extracted. In the NA group, rats would be taken away immediately, without performing any further tests beforehand, to get their brains extracted (BE). This figure was created using Google Drawings (2022).

2a)



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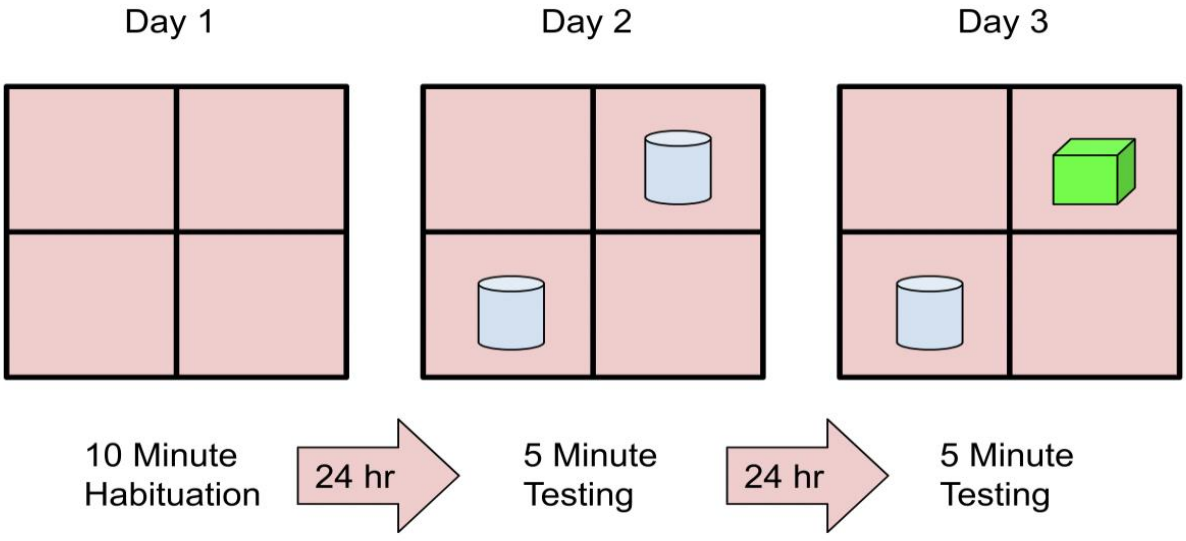

Figure 2. The experimental paradigms. 2a) An in-depth schedule of the strict exercise protocol that groups Aβ+6E, and C+6E would be following over the course of 6 weeks. Groups Aβ+1E and C+1E would only be exposed to 1 week of exercise following the schedule for week 6. Groups Aβ and C would not be exposed to the exercise regimens at all. 2b) The 3 day NOR experimental protocol that the NOR group rats would be introduced to one day after exercise. During day 1, the rats would be given a 10-minute habituation period to get familiarized with the environment. On days 2 and 3, the rats would be participating in testing for 5 minutes each day, exposed to the same or different objects, respectively. The rats would be given a 24-hour rest period in their home cages, before returning to the cage each day. This figure was created using Google Drawings (2022).

Magnetic Resonance Imaging (MRI)

One day after the aerobic exercise was complete, the MRI group would be taken to an MRI facility to visualize hippocampal structure, volume and matter (Figure 1). During this time the rats would be lightly anesthetized and held still, using a fixed head holder and flexible textile, following the Wolf et al methodology [11]. The scans would take approximately 70 minutes per rat [11].

Aβ peptide, P-Tau and BDNF Level Measurement

Once the MRI scans and NOR tests were acquired, all 48 rats in the NOR group, MRI group and NA group would be sacrificed, and their brains would be extracted. The hippocampus would be isolated, dissected and stored, kept at -80°C following the Nigam et al methodology [12]. The cells would be cultured and levels of Aβ would be measured in cell culture media [12]. Immunofluorescence labeling would be used to detect the protein expression levels of p-tau following the Yang et al methodology [5]. BDNF in frozen rat cortical tissue lysates would also be measured using BDNF ELISA immunoassays [11]. These measurements would then be recorded and evaluated.

Statistical Analysis

All of the data would be presented as mean ± standard deviation (SD) [4]. Statistical comparisons would be made using SPSS 23.0, a statistical software package [4]. Following the Fakhraei et al methodology, a one-way ANOVA test would be used to compare the variables between the three studied groups of rats [1]. Significance between variables would be considered at the level of $P \leq 0.05$ [1]

Results

Protein level Assays

Within the control groups (C, C+1E and C+6E), it can be hypothesized that the C and C+1E groups would show slightly lower levels of BDNF in the hippocampus in comparison to the C+6E group. Within the AD induced group (Aβ, Aβ+1E and Aβ+6E), it can be predicted that the Aβ+6E group would show significantly greater BDNF levels in the hippocampus when compared to the Aβ and Aβ+1E groups. When comparing the BDNF levels in the hippocampus of the control groups to the AD induced groups, it can be assumed that hypothetically the control groups would overall show a significantly greater level of BDNF in the hippocampus compared to the non-control groups. This is similar to the findings of the studies conducted by Shamsipour et al and Fakhraei et al, in which they described a significant increase in the BDNF mRNA levels in the hippocampus of the Aβ+exercise group compared to the Aβ group [3,4]. It can be estimated that the AD induced groups (Aβ, Aβ+1E and Aβ+6E) would show significant differences in levels of p-tau and Aβ amongst one another, with much greater levels of Aβ and p-tau present in the Aβ and Aβ+1E groups, compared to the Aβ+6E group. It can also be hypothesized that the control groups, (C, C+1E and C+6E), would show no significant differences in levels of p-tau and Aβ amongst one another, but would show much lower levels of Aβ and p-tau in comparison to the AD induced groups (Aβ, Aβ+1E and Aβ+6E). Hypothetically, when comparing the presence of differing amounts in Aβ and p-tau levels, there would be a greater difference between the control groups and the Aβ and Aβ+1E groups, and less of a difference between the control groups and the Aβ+6E group. The studies conducted by Nigam et al and Zhang et al found similar results, in which they found decreased levels of Aβ and p-tau in the hippocampus of the Aβ injection + exercise group, compared to the Aβ injection group, and increased levels of Aβ and p-tau in the hippocampus, compared to the control group [3,13].

Behavioural

It can predicted that within the NOR group, the Aβ and Aβ+1E groups would spend significantly less time exploring the novel object, and more time exploring the old object, compared to the Aβ + 6E, C, C+1E and C+6E groups. The study conducted by Farzi et al demonstrated similar findings, in which the control groups showed no significant difference in the memory index, whereas the Aβ injected group showed lower novel object exploring time compared to the control groups and the Aβ + aerobic exercise group showed greater novel object exploring time compared to the Aβ injected group. [12].

Structural

It can be predicted that within the MRI group, the MRI would show a significant decrease in hippocampal volume and gray matter in the hippocampus of the Aβ and Aβ+1E groups compared to the Aβ+6E group. Contrastingly, it would be anticipated that the C and C+1E groups would show no significant differences in hippocampal volume and gray matter when compared to one another, while the C+6E groups would show increased hippocampal volumes. It can be anticipated that when comparing the control to the AD induced groups, there would be overall greater levels of hippocampal volume and gray matter in the control groups. More specifically, it would be anticipated that the Aβ and Aβ+1E groups would have significantly less hippocampal volume and gray matter compared to any of the control groups, while the Aβ+6E group may not be significantly different, but still less than the control groups. Studies conducted by Parent et al and Erikson et al also found results similar, in which their MRI findings showed a significant decrease in the hippocampal volume of the Aβ injection group when compared to the Aβ injection + exercise and control groups [13, 14].

Discussion

Aβ peptides are one of the most significant pathologic features associated with AD in rats, being highly associated with the cognitive decline and AD [4]. Within this study it was hypothesized that the rats who were injected with Aβ

and thereby AD induced, would perform worse on the NOR tests compared to the rats who were instead injected with saline. This could be due to the formation of toxic aggregations as a result of Aβ peptide accumulation in the hippocampus [4,9]. These toxic aggregations can encourage the production of NFTs, as well as other insoluble plaques in varying sizes, which can attribute to cognitive decline by decreasing the number of neural cells and synapses in the hippocampus [4,9]. Hence, when injected with Aβ peptides, the rats would have experienced cognitive decline, as their short-term memory recognition would have been negatively impacted by the formation of NFT's and other insoluble plaques, leading to defective memory formation and causing them to hypothetically perform poorly on the NOR test.

Although NFT'S are associated with cognitive decline in rats with AD, many studies have shown that the cognitive decline may potentially be reduced through lifestyle changes, such as regular exercise [2,4,9]. Within this study it was predicted that the Aβ+6E rats would have performed better on the NOR tests compared to the Aβ and Aβ+1E rats. Although all of the rats would have been injected with Aβ peptides, only one of the groups would be expected to show improved cognition, with the differentiating factor being the exercise regimens. Regular exercise has been known to stimulate an increased expression of BDNF gene production within the hippocampus [4]. BDNF is a protein involved in neuroprotection, as well as neuronal survival, resilience and restoration [2]. BDNF also works in reducing cognitive decline by limiting the production of Aβ peptides, which are highly associated with the cognitive decline in rats with AD [3]. Aβ peptides are released from amyloid precursor proteins (APPs), which is enabled through the β -secretase enzyme activity [3]. BDNF functions by triggering a downstream inhibition pathway of β -secretase, through enhanced α-secretase activity. APP is cleaved by α-secretase, which releases a neuroprotective secreted form of APP (sAPPα), and in turn stops β -secretase from cleaving APP, in order to prevent generating Aβ [3]. Essentially, BDNF is released through regular exercise, and not only works as a neuroprotectant in itself, but it inhibits Aβ peptide production, reducing the cognitive decline associated with AD. Thus, with the most consistent exercise having hypothetically been done by the Aβ+6E group, it is expected that they would have the greatest levels of BDNF, and lowest levels of Aβ peptides and p-tau, compared to the Aβ and Aβ+1E groups. Hence, the Aβ+6E group would have the best NOR behavioural results, as they are the least impacted by the AD symptoms induced by the Aβ injection.

While the NOR test is a method in which the cognitive decline associated with AD in rats can be assessed behaviourally, structural changes can be evaluated through MRI testing. The hippocampus is widely known for being associated with memory processes, thus a lack of hippocampal volume and gray matter can be associated with impaired memory processes [15]. Within this study it was predicted that the Aβ+6E rats would show greater gray matter and hippocampal volume in the MRI, compared to the Aβ and Aβ+1E rats. This is because Aβ peptides have been associated with potentially leading to a significant decrease in hippocampal volume and gray matter in rats with AD, due to cell death as a result of Aβ toxicity, which has been confirmed through MRI testing [13]. The lack of exercise that would have been performed by the Aβ and Aβ+1E groups, would result in increased levels of Aβ peptides, in comparison to the Aβ+6E rats, which would align with the predicted results from the protein level measurements [3]. Thus, the increased levels of Aβ peptides, resulting in greater amounts of cell death, would explain the decreased hippocampal volume and gray matter present, for the Aβ and Aβ+1E groups in the MRI [13]. Meanwhile, the Aβ+6E rats would be expected to show greater levels of BDNF due to their increased exercise, in comparison to the Aβ and Aβ+1E groups, which would once again align with the expected results from the protein level measurement [2,4]. The increased levels of BDNF expected in the Aβ+6E group, would inhibit Aβ cleavage as previously described, resulting in better cell health due to reduced Aβ toxicity [3,13]. This in turn would explain the anticipated greater amounts of gray matter and hippocampal volume present, for the Aβ+6E group in the MRI. Thus, with regular exercise increasing BDNF gene expression, and limiting the presence of Aβ peptides in the hippocampus, it can be assumed that regular exercise could potentially reduce hippocampal volume and gray matter loss in rats with AD [9].

Conclusions

To conclude, the present study suggests that regular exercise and lifestyle changes could be associated with the reduced progression of cognitive decline in rats with AD. AD induced rats who participate in regular exercise, could exhibit improved cognition, both structurally and behaviourally, in comparison to rats with AD, who do not participate in regular exercise. Although the findings within the present study focused largely on rats, it is important to think about how the research presented can be applied, and contribute, to potentially translating over to therapeutic treatments for AD in humans. Thus, partaking in regular exercise can be an incredibly affordable and accessible lifestyle adaptation that can potentially be used by the widespread population, in order to aid in reducing the cognitive decline associated with AD.

List of Abbreviations Used

AD: Alzheimer's disease
Aβ: amyloid-beta
APP: amyloid precursor protein
sAPPα: secreted amyloid precursor protein
BDNF: brain derived neurotrophic factor
MRI: magnetic resonance imaging
NFTs: neurofibrillary tangles
NOR: novel object recognition
P-tau: *phosphorylated* tau protein

Conflicts of Interest
The author declares that they have no conflict of interest.

Ethics Approval and/or Participant Consent
This study did not require ethics approval and/or participant consent as it is a experimental proposal that analyzed and interpreted journal articles.

Authors' Contributions
RM: made substantial contributions to the design of the study, the collection of data as well as interpretation and analysis of the data, revised the manuscript critically, and gave final approval of the version to be published.

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References
[1] Fakhraei S, Almasi MR, Peeri M, Gharakhanlou R. The effect of 4-week rehabilitation by aerobic exercise on hippocampus BDNF and TGF-B1 gene expressions in AB 1-42 -induced rat model of Alzheimer's disease. Journal of Clinical Neuroscience. 2022 Jan; 95:106-111. https://doi.org/10.1016/j.jocn.2021.11.027
[2] Diniz BS, Teixeira AL. Brain-derived neurotrophic factor and Alzheimer's disease: Physiopathology and Beyond. Neuromol Med. 2011 Sept 7; 13:217-222. https://doi.org/10.1007/s12017-011-8154-x
[3] Nigam SM, Xu S, Kritikou JS, Marosi K, Brodin L, Mattson MP. Exercise and BDNF reduce Aβ production by enhancing α-secretase processing of APP. J Neurochem. 2017 Jul;142(2):286-296. http://dx.doi.org/10.1111/jnc.14034
[4] Shamsipour S, Sharifi G, Taghian F. Impact of interval training with probiotic (L. plantarum / Bifidobacterium bifidum) on passive avoidance test, ChAT and BDNF in the hippocampus of rats with Alzheimer's disease. Neuroscience Letters. 2021 Jun 21;756. https://doi.org/10.1016/j.neulet.2021.135949
[5] Yang Y, Hu S, Lin H, He J, Tang C. Electroacupuncture at GV24 and bilateral GB13 improves cognitive ability via influences the levels of Aβ, p-tau (s396) and p-tau (s404) in the hippocampus of Alzheimer's disease model rats. NeuroReport. 2020 Oct 14;31(15):1072-1083. http://dx.doi.org/10.1097/WNR.0000000000001518
[6] Cohen RM, Rezai-Zadeh K, Weitz TM, Rentsendorj A, Gate D, Spivak I, Bholat Y, Vasilevko V, Glabe CG, Breunig JJ, Rakic P, Davtyan H, Agadjanyan MG, Kepe V, Barrio JR, Bannykh S, Szekely CA, Pechnick RN, Town T. A transgenic Alzheimer rat with plaques, tau pathology, behavioral impairment, oligomeric aβ, and frank neuronal loss. J Neurosci. 2013 Apr 10;33(15): 6245-56. https://doi.org/10.1523/jneurosci.3672-12.2013
[7] Jullienne A, Trinh M.V, Obenaus A. Neuroimaging of mouse models of Alzheimer's disease. Biomedicines. 2022 Jan 28;10(2):305. http://dx.doi.org/10.3390/biomedicines10020305
[8] Luo L, Li C, Du X, Shi Q, Huang Q, Xu X, Wang Q. Effect of aerobic exercise on BDNF/proBDNF expression in the ischemic hippocampus and depression recovery of rats after stroke. Behavioural Brain Research. 2019 Apr 19;362:323-331. https://doi.org/10.1016/j.bbr.2018.11.037
[9] Xianliang Z, Qiang H, Tao H, Na Z, Fei L, Bo X, Xianghe C, Tuojian L, Jianzhong B. Treadmill exercise decreases Aβ deposition and counteracts cognitive decline in APP/PS1 mice, possibly via hippocampal microglia modifications. Frontiers in Aging Neuroscience. 2019 Apr;11. https://doi.org/10.3389/fnagi.2019.00078
[10] Wan H, Aggleton JP, Brown MW. Different contributions of the hippocampus and perirhinal cortex to recognition memory. J Neurosci. 1999 19:1142–1148. https://doi.org/10.1523/JNEUROSCI.19-03-01142.1999
[11] Wolf OT, Dyakin V, Patel A, Vadasz C, de Leon MJ, McEwen BS, Bulloch K. Volumetric structural magnetic resonance imaging (MRI) of the rat hippocampus following kainic acid (KA) treatment. Brain Res. 2002 May 3;934(2):87-96. http://dx.doi.org/10.1016/S0006-8993(02)02363-6
[12] Farzi MA, Sadigh-Eteghad S, Ebrahimi K, Talebi M. Exercise improves recognition memory and acetylcholinesterase activity in the beta amyloid-induced rat model of Alzheimer's disease. Ann Neurosci. 2018 Apr 12;25(3):121-125. https://doi.org/10.1159/000488580
[13] Parent MJ, Zimmer ER, Shin M, Kang MS, Fonov VS, Mathieu A, Aliaga A, Kostikov A, Carmo SD, Dea D, Poirier J, Soucy J, Gauthier S, Cuello AC, Rosa-Neto P. Multimodal imaging in rat model recapitulates Alzheimer's disease biomarkers abnormalities. J Neurosci. 2017 Dec 13;37(50):12263-12271. http://dx.doi.org/10.1523/JNEUROSCI.1346-17.2017
[14] Erickson KI, Leckie RL, Weinstein AM. Physical activity, fitness, and gray matter volume. Neurobiol Aging. 2014 Sep;35 Suppl 2:S20-8. http://dx.doi.org/10.1016/j.neurobiolaging.2014.03.034

[15] Huijbers W, Mormino EC, Schultz AP, Wigman S, Ward AM, Larvie M, Amariglio RE, Marshall GA, Rentz DM, Johnson KA, Sperling RA. Amyloid-β deposition in mild cognitive impairment is associated with increased hippocampal activity, atrophy and clinical progression. Brain. 2015 Apr;138(Pt 4):1023-35. https://doi.org/10.1093/brain/awv007

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