TOWSON UNIVERSITY
OFFICE OF GRADUATE STUDIES

THE ROLE OF SIMVASTATIN IN PREVENTING DIET-INDUCED COGNITIVE

DECLINE

by

Christopher J. Wayman

A thesis

Presented to the faculty of

Towson University

in partial fulfillment

of the requirements for the degree

Masters of Arts

Department of Psychology

Towson University
Towson, Maryland 21252

May 2017

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THESIS APPROVAL PAGE

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Role of Simvastatin in Preventing Diet-Induced

Cognitive Decline

has been approved by the thesis committee as satisfactorily completing the thesis
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Paul Pistell	Paul Pistell	4/20/2017
Chairperson, Thesis Committee Signature	Type Name	Date
Bryan Devan	Bryan Devan	4/20/2017
Committee Member Signature	Type Name	Date
M. Paz Galupo	M. Paz Galupo	4-20-17
Committee Member Signature	Type Name	Date
Committee Member Signature	Type Name	Date
Committee Member Signature	Type Name	Date
Janet V. DeLany	Janet V. DeLany	5-2-17
Dean of Graduate Studies	Type Name	Date

Abstract

The Role of Simvastatin in Preventing Diet-induced Cognitive Decline

Christopher J. Wayman

The introduction of processed sugars and fats as the macronutrient foundation for many foods has played a contributing role in the increased incidence of heart disease. Likewise, chronic consumption of this "Western"-style may have a significant negative impact on healthy cognitive function. Statins may have unique neuroprotective agency in cases of cognitive decline associated with chronic consumption of the Western diet. The current study examined the effects of long-term high-fat diet consumption in a rodent sample to ultimately explore the effectiveness of Simvastatin in preventing potential cognitive decline. No significant effects of diet nor of Simvastatin treatment were revealed. A significant effect of diet on Rotarod performance was found, such that high-fat diet mice performed worse than mice treated with Simvastatin and control mice. Further exploration of both high-fat diet and Simvastatin treatment paradigms are necessary to construct a more secure bedrock for future research in this area.

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Literature Review

Introduction

Within the past decade, there has been flourishing interest in the effects of high-fat and high-cholesterol diets notably due to a steady increase of obesity incidence within Eurocentric populations (Drewnowski, 2000). Nearly two-thirds of the American population is overweight, and many studies suggest that this may be consequential of an increased consumption of high-fat- and high-carbohydrate-based diets prevalent in many Western cultures (Freeman, Haley-Zitlin, Rosenberger & Granholm, 2014). And although excess body fat entails numerous risk factors for physiological disease, current research suggests that increased consumption of the "Western" diet may lead to neurological changes, neurodegenerative disorders and plasma cholesterol modulation which may inhibit healthy cognitive function. (Stranahan, Cutler, Button, Telljohann & Mattson, 2011). Emerging research suggests that the application of statin regimens, a class of drug which evidently modulates blood plasma cholesterol levels, may reduce oxidative stress and neuroinflammatory symptoms purportedly responsible for reduced cognitive function associated with long-term consumption of the Western diet (Ramirez, Tercero, Pineda & Burgos, 2011; Miller & Spencer, 2014).

A substantial amount of research has been conducted which attempts to evaluate some of the principle neuroscientific phenomena associated with the effect of diet on psychological function, chiefly the interactions between diet modulation and consequent cognitive impairment. Likewise, within recent years, an impressive amount of research has been conducted which questions the efficacy of statin regimens to reduce many of the negative health risks associated with the Western diet and evaluates their neuroprotective agency in the treatment of associated cognitive decline.

The current study focuses on both the effects of chronic high-fat diet consumption on cognitive decline in a rodent population and the potential neuroprotective effects of Simvastatin as a pharmaceutical intervention. Specifically, the current study measures the effects of chronic high-fat diet consumption as observed via relevant literature and through novel experimental design. The purpose of this study is to first examine how mice fed an exclusively high-fat diet and tested in the Stone-T Maze and Rotarod apparatus compare to mice fed a normal diet. Likewise, this study examines how treatment with Simvastatin may persuade behavioral testing for mice fed a high-fat diet versus a normal diet. Forward, this review navigates these topic areas and synthesizes contemporary research to show the effects of diet-induced cognitive decline and the neuroprotective agency of statins.

Western Diet and Obesity

Since the Neolithic Revolution, humans have undergone a relatively drastic change in diet composition. The innovation of progressively advanced agricultural and farming techniques has allowed humans abundant access to foods like refined

carbohydrates and processed dairy otherwise inaccessible to most other species. This innovation, although historically imperative for the survival of our species, may likewise be responsible for some of our most physically and neurologically damaging diseases (Francis & Stevenson, 2013).

Most of the world now lives in a time when low-cost and calorically dense foods are readily available for purchase at convenience, especially for Western nations where fast food is a common dietary staple generally due to affordability and caloric density (Drewnowski, 2004). These foods which compose the "Western" diet typically combine processed sugars, saturated fats and red meats, macronutrients atypical of the paleo-like diets consumed in many Eastern nations (Drewnowski, 2000) composed of complex carbohydrates and lean proteins.

The Western diet is also more likely to contain multiple preservatives, additives and undergo rigorous processing before consumption (Freeman et al., 2014). Appropriately, chronic Western diet consumption has been linked to obesity, among other diseases, and obesity incidence in the Western world continues to radically increase. In the United States alone, 28.3% of adults are currently classified as clinically obese (Centers for Disease Control and Prevention, 2015). This statistic has startling implications for the overall health of any nation considering established links between obesity and cardiovascular disease, Type-2 diabetes and dyslipidemia, among many other life-threatening diseases (Malnick & Knobler, 2006).

Recent research also shows significant comorbidity between obesity and cognitive dysfunction (Francis & Stevenson, 2013; Kanoski, Zhang, Zheng & Davidson, 2010).

Cognitive impairments and neurological damage associated with poor diet may be expressed as early as adolescence, potentially impacting neuroplasticity and reward-processing pathways (Reichelt, 2016). Research also suggests that chronic unhealthy dietary consumption in childhood and adolescence may yield synaptic dysfunction later into adulthood (Wang et al., 2015). Appropriately, there is an emerging body of literature which suggests that the macronutrient composition of the Western diet may directly modulate cognition and behavior (Cordner & Tamashiro, 2015). Many studies conducted with rodent populations consistently show that both mice and rats perform worse on behavioral tasks following chronic consumption of high-fat diets blended to emulate the Western diet (Gainey et al., 2016). Beyond baseline behavioral deficits, extended consumption of the Western diet in rodent-based experimental studies have resulted in an observed reduction of working memory (Freeman, Haley-Zitlin, Rosenberger & Granholm, 2014) and spatial-recognition memory after just 9 weeks of diet exposure, as well as mounting evidence that the Western diet may be linked to changes in dopamine levels (Nguyen et al., 2017), depressive behaviors and poor immune response (Andre, Dinel, Ferreira, Laye & Castanon, 2014).

Oxidative Stress

Perhaps one of the most influential components on cognitive deficits associated with Western diet consumption and obesity is the increased incidence of oxidative stress, a cellular process wherein unbound free-radical molecules trigger atypical immune responses in otherwise healthy neurons (Oliver et al., 2010). Chronic oxidative stress as a result of frequent high-fat consumption may therefore yield neurotoxic effects on the brain and may even cause entire regions to undergo neurological changes (Francis & Stevenson, 2013) and eventually lead to cognitive decline (Freeman et al., 2014).

Frequent exposure to oxidative stress is likewise accompanied by atypical neuro-inflammation (Pistell et al., 2010), an immune response characterized by an over-activation of cytokines, proteins which modulate basic immune system function (Oliver et al., 2010). This atypical cytokinetic activation has been shown to trigger gliosis and unhealthy cellular inflammation (Ramirez et al., 2011).

It is now known that the amount of serum cholesterol, or the amount of cholesterol measurable at any given time in the blood stream, may act as a predictor for many of these aforementioned neurodegenerative conditions (Ramirez et al., 2011), working memory deficits (Freeman et al., 2014) and even damage to the blood brain barrier (Hargrave, Davidson, Lee & Kinzig, 2015), among increased propensity for amyloid-β upregulation (Morley & Banks, 2010), a chief contributor to Alzheimer's disease (Granholm et al., 2008). Appropriately, there is a well-established link between the consumption of high-fat diets and serum cholesterol levels (Granholm et al., 2008) and, more specifically, the Western diet and serum cholesterol levels (Stranahan et al.,

2011). Most research suggests that diet-induced cholesterol changes result from an increase in lipid metabolism (Stranahan et al., 2011). In light of this evidence, HMG-CoA reductase inhibitors, or statins, have gained recent momentum in Western healthcare.

Statins and Diet

Statins are primarily used to lower serum cholesterol by inhibiting the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, an enzyme chiefly responsible for the synthesis of cholesterol in the bloodstream (Lee, Won, A. Singh & I. Singh, 2008). Without HMG-CoA reductase, cells cannot synthesize cholesterol from dietary lipids. Hence, the application of statins has been shown to reduce overactive cellular synthesis of cholesterol in the bloodstream (Li, Cao, Kim, Lester & Fukuchi, 2006) and therefore may reduce the risk of cardiovascular disease (Dolga et. al., 2009) associated with heightened serum cholesterol levels often associated with chronic consumption of the Western diet. However, in recent years, statins have also shown a number of neuroprotective benefits outside of cholesterol modulation.

Research regarding the effects of statins on neurological function are still relatively new, having only emerged within the past decade or so. However, there is already an impressive amount of literature which establishes a potential neuroprotective basis for the application of statin treatment regimens and their beneficial effects on neuron health and cognition (Ghodke, Tour & Devi, 2012).

Outside of their primary purpose, many statins have been shown to reduce the amount of oxidative stress occurring within the brain (Kurata et. al., 2011). Similarly, statins have also been shown to reduce nueroinflammation and subsequent neurotoxicity (Kurata et. al., 2011). Statin treatments have even shown certain neuroprotective and neurogenerative agency in cases of brain trauma (Lu et. al., 2007).

Unfortunately, the vehicle through which all of these neuroprotective phenomena act is still left to speculation. However, because there are many different types of statins currently used in clinical application, researchers have begun conducting experiments which analyze differences between statin variations. Specifically, researchers have started examining novel effects of different statin characteristics based on molecular diversity (Ramirez et al., 2011). As a result, one proposed attribute of effective neuroprotective quality which varies between statin types is their pharmacological solubility, either lipophilic or hydrophilic. It is now understood that the statins which most effectively prevent neuroinflammation and oxidative stress in the central nervous system are lipophilic, fat-soluble and can freely pass through the blood brain barrier (Ghodke et al., 2012). One of the most effective statin treatments on the market today, Simvastatin, is among the most lipophilic (Ghodke et al., 2012) and has numerous neuroprotective characteristics.

Simvastatin and Cognition

Simvastatin, trade name Zocor, is a statin which has been frequently studied due to its lipophilicity. Because Simvastatin is readily able to pass the blood brain barrier once introduced to the body, it can act directly on the central nervous system. This has

shown particularly beneficial in deterring cognitive deficits (Vandresen-Filho et al., 2015) associated with oxidative stress and neurotoxicity (Kurata et al., 2011). Simvastatin treatment may also enhance long-term potentiation central to hippocampal-based learning and memory (Mans, Chowdhury, Cao, McMahon & Li, 2010) and improve performance on other behavioral tasks (Can, Ulupinar, Ozkay, Yegin & Ozturk, 2012).

In an experiment by Ramirez et al., (2011), Kainic acid, a powerful neurotoxin used for excitotoxicity lesioning, was administered to lab mice. During administration of Kainic acid, experimental groups were given different variations of statins and then tested on a number of behavioral and pharmacological factors. Ramirez et al. (2011) found that Simvastatin was the most effective neuroprotective agent against kainate-induced excitotoxicity. Further, Ramirez et al. (2011) extrapolated that Simvastatin may act as an antioxidant, protecting against the harmful effects of chronic Western diet consumption like oxidative stress and neuroinflammation. The antioxidant effects of Simvastatin have been documented in other research as well (Franzoni, Quinones-Galvan, Regoli, Ferrannini & Galetta, 2003), as well as its deterrence of neuroinflammation (Kurata et al., 2011). Along with the already noted benefits of Simvastatin, research now suggests that treatment in combination with other preventative drugs may reduce Alzheimer's expression (Papadopoulos, Tong & Hamel, 2014; Wolozin, Kellman, Ruosseau, Celesia & Siegel, 2000) and the behaviors associated with the disease (Kou et al., 2010).

Stone T-Maze

Given the experimental demands of dietary and pharmaceutical research, animal samples are commonly utilized. Finding human participants to conduct statin treatment

research upon is challenging simply because it is difficult to find human participants in an undergraduate cohort that do not consume a Western-like diet, thus restricting the pool of control participants. Therefore, much of the research surrounding this topic area is conducted with rodent populations. An animal sample will thus be utilized in the present study. Research with rodents also allows for histology and immunohistochemistry following treatment, forms of analysis impossible to execute in assessing damage in living human participants.

Many studies which test the behavioral benefits of Simvastatin treatment in rodent populations vary methodologically. One relevant testing apparatus is the Stone T-maze, a mouse-oriented maze which is thought to access procedural learning and egocentric movement (Pistell et. al., 2009). Therefore, cognitive deficits are theoretically visible in the Stone T-maze, observable through error reduction from between trials. The Stone T-maze is also considered a relevant measurement tool for damage caused by oxidative stress (Duffy et. al., 2008), an especially pertinent feature for this subject area and further inquiry.

To conclude, although a substantial amount of research has been conducted featuring the neuroprotective agency of statins, specifically Simvastatin, on cognition from chronic Western diet consumption, there are still many gaps in the theoretical and pharmacological domains which need to be filled. Researchers have proposed many mechanisms for the effects of Statins, but further research is necessary to compile more substantive neurological and behavioral evidence appertaining to the specificity of effects. This review navigates only a small selection of topic areas interconnected within

this field to synthesize them and establish a greater foundation of knowledge, but as health care continues to develop in Western nations to address the growing obesity epidemic, cardiovascular-related morbidity and even Alzheimer's disease, drugs of this nature will only become more relevant to the psychological well-being of humans in the foreseeable future and demands further inquiry.

Hypotheses

Because research on the effectiveness of Simvastatin as an intervention treatment in reducing cognitive decline remains at the moment relatively underdeveloped, further research is necessary to expand upon preexisting experimental iterations and ultimately bridge gaps within the existing body of research in this area. This study utilized a 3x5 repeated measures design using three exclusive groups of mice – one group fed a high-fat diet, one group fed a high-fat diet but given Simvastatin, and a third control group; all tested over five trial blocks – to examine the effects both a high-fat diet and treatment with Simvastatin yield on cognition measured through behavioral testing via the Stone-T Maze and Rotarod apparatus.

Considering evidence that statin regimens may reduce oxidative stress and diet-induced neuroinflammation as a causal factor in cognitive decline associated with Western diet consumption (Francis & Stevenson, 2013), I hypothesized that mice fed a supplemented high-fat diet will show behavioral deficits indicative of cognitive decline. Further, I also hypothesized that an intervention treatment regimen of Simvastatin will reduce behavioral deficits associated with cognitive decline consequential of long-term high-fat diet consumption. Ultimately, rationale for these hypotheses was to both

reinforce the current model for diet-induced cognitive decline in mice and to show that

the use of Simvastatin as an intervention treatment may have a positive effect on

cognitive function, ideally providing important empirical evidence which may translate to

clinical application in the future.

Methods

Subjects

The subjects for this experiment were 36 C57BL/6 all-male lab mice. All mice

were bred in-house for the sole purpose of experimental use. Mice were housed in a

temperature- and humidity-controlled room with a 12-hour light/dark cycle. All

treatments and behavioral testing had occurred during the automatically regulated 12-

hour light cycle.

Procedure

Two experimental groups of 12 randomly assigned mice were fed a pre-milled high-fat diet blend as a supplemented food source for approximately 10 weeks while a third control group of 12 mice retained a normal lab chow diet during that same time. The Simvastatin treatment group was given Simvastatin through intraperitoneal (IP) injection once daily for approximately 7 days. Simvastatin treatment followed a 20mg/kg dosage dissolved in DMSO then suspended in Tween and saline for IP administration, yielding approximately 0.50 mg daily Simvastatin per mouse for a period of one week (see Table 1). The untreated experimental group was not given Simvastatin, only the high-fat diet. Both treated and untreated experimental groups had ad lib access to only the high-fat diet chow for the 10-week duration of this study. Following completion of Simvastatin treatment, all groups underwent behavioral testing in the Stone T-Maze and the Rotarod performance test.

Stone T-Maze

The apparatus used to test cognitive decline for this study was the Stone T-maze. The Stone T-maze consists of a series of passages paired with multiple routes, appropriately measuring latency and error rate and thus learning. During trials, mice were caused to wade through water, an aversive stimulus which creates motivation to progress. Mice were familiarized with the Stone T-maze through training on a straight-run apparatus of similar construct prior to experimental maze trails one day prior to Stone T-Maze testing. During the straight run task, mice were required to navigate a straight path to the goal box to show that learning had taken place before Stone T-maze trials. During

the Stone T-Maze trial blocks, each subject in all conditions ran the maze 15 times divided into 5 trial blocks, thus three trials per mouse per block. Any trial exceeding 300 seconds was considered a failed trial.

Given the hypothesis for this experiment, initially, a higher error rate was expected when comparing experimental groups to the control group. Following treatment, a decreased error rate was hypothesized to occur within the high-fat diet group receiving Simvastatin treatment but not for mice exclusively fed the high-fat diet.

Rotarod

Rotarod testing was carried out for all groups in one session. The main purpose of Rotarod testing was to measure any potential motor or cognitive impairment between groups. Mice were required to maintain hold of a rod as it rotates at progressively increasing rotations per minute. Duration spent on the Rotarod was collected for each individual mouse upon falling from the rod. In scope of the present experimental groups, Simvastatin-treated mice were expected to perform better on the Rotarod task than the untreated group, but both experimental groups fed the high-fat diet were expected to perform worse than the control group.

<div align="center">

Results

</div>

A repeated-measures analysis of variance revealed a significant between-group effect of diet on weight, $F(2, 33) = 13.25$, $p < .001$, $\eta^2 = .445$, power = .995 [90% C.I.: 0.20, 0.58], such that both high-fat diet treated groups (treatment and no treatment) weighed significantly more than the control mice consistently over the diet exposure period (see Figure 1).

A one-way ANOVA revealed a significant effect of diet on Rotarod latency, $F(2,$ 35) = 4.414, p = .020, η^2 = .201, power = .760 [90% C.I.: 0.02, 0.35], (see Figure 2). A Bonferroni post-hoc analysis showed that high-fat diet mice without Simvastatin treatment spent significantly less time on the Rotarod than the control group (M = 35.78, SE = 12.83).

A repeated-measures ANOVA revealed neither a significant effect of Stone T-Maze acquisition latency, $F(2, 27)$ = 0.05, p = .951, η^2 = .004, power = .057 [90% C.I.: 0.00, 0.05] (see Figure 3); nor did it reveal a significant effect of Stone T-Maze acquisition error across groups, $F(2, 27)$ = 0.20, p = .821, η^2 = .015, power = .078 [90% C.I.: 0.00, 0.10], (see Figure 4).

Discussion

Although the Stone T-Maze acquisition trials did not show any significant group differences in learning neither within error nor latency measures, the results are nonetheless worth discussing. Freeman et al. (2014) previously established that oxidative stress as a precipitated of Western diet consumption negatively impacts rodent performance on behavioral tasks. The current study attempted to validate that argument by eliciting diet-induced oxidative stress.

The repeated-measures ANOVA for group latency in the Stone T-Maze neither revealed a significant difference between amount of time it took groups of mice to complete the maze, nor did the ANOVA reveal a significant group difference between amount of errors committed over the 15-trial period. One possible explanation for this result is that mice had not been exposed to the high-fat diet for a long enough duration.

Although mouse weight significantly increased between high-fat diet and control diet groups, perhaps the treatment effect was not robust enough to elicit strong enough cognitive deficits to yield behavioral performance disparity between groups. Through their research, Francis & Stevenson (2013), found that physiological changes resulting from chronic oxidative stress can take up to 6 months to manifest, which is nearly double the amount of time the current study employed for diet exposure. This may explain why although high-fat mice performed significantly worse on the Rotarod, a motor-performance task, mice did not show pronounced cognitive deficits which we would expect to see in error rate differences between high-fat and control groups.

Given the lack of robust effect of high-fat diet exposure on cognitive degeneration, it is consequentially difficult to substantiate conclusions regarding Simvastatin treatment. Because no significant behavioral differences between dietary groups were observed, it may therefore be impossible to suggest that the Simvastatin was preventing cognitive dysfunction at all, as mice lacked the intended deficits which the Simvastatin intervention intended to prevent. That is to say, if no changes occurred as a result of diet exposure, then the effect of the Simvastatin treatment becomes redundant in discussion.

One possible explanation for lack of diet effect neglecting truncated exposure duration may involve the actual macronutrient composition of the applied high-fat supplemented diet. The high-fat diet chosen for this study mainly utilizes coconut oil as the macronutrient foundation. In future research, perhaps a more carbohydrate-based dietary blend may yield more robust behavioral manifestations of oxidative stress, as research has shown that a more carbohydrate-rich diet closely emulating the Western Diet

likely yields significant deficits as a result of neuroinflammation in mice (Andre et al., 2014). Aside from behavioral effects, this study was unfortunately limited in its capacity to investigate histological differences between high-fat, treatment and control groups, barring physiological comparison of potentially affected brain regions. Although not critical, this certainly may have provided a look into potential physiological changes even though no significant cognitive deficits arose.

Although this study only found marginally significant results, this study foremost acted as a necessary pilot for future dietary and drug intervention research and likewise prompted the planning and execution of essential processes in the research process. In that capacity, this study was successful. Ultimately, this study showed that robust behavioral deficits resulting from high-fat diet exposure likely rely on exposure duration. This study also showed that mice exposed to a high-fat diet perform significantly worse on Rotarod performance. Although limited, these findings help to establish how dietary differences affect cognitive and motor ability in mice.

Appendix A: Tables and Figures

Table 1

Treatment Duration and Dosage Per Group

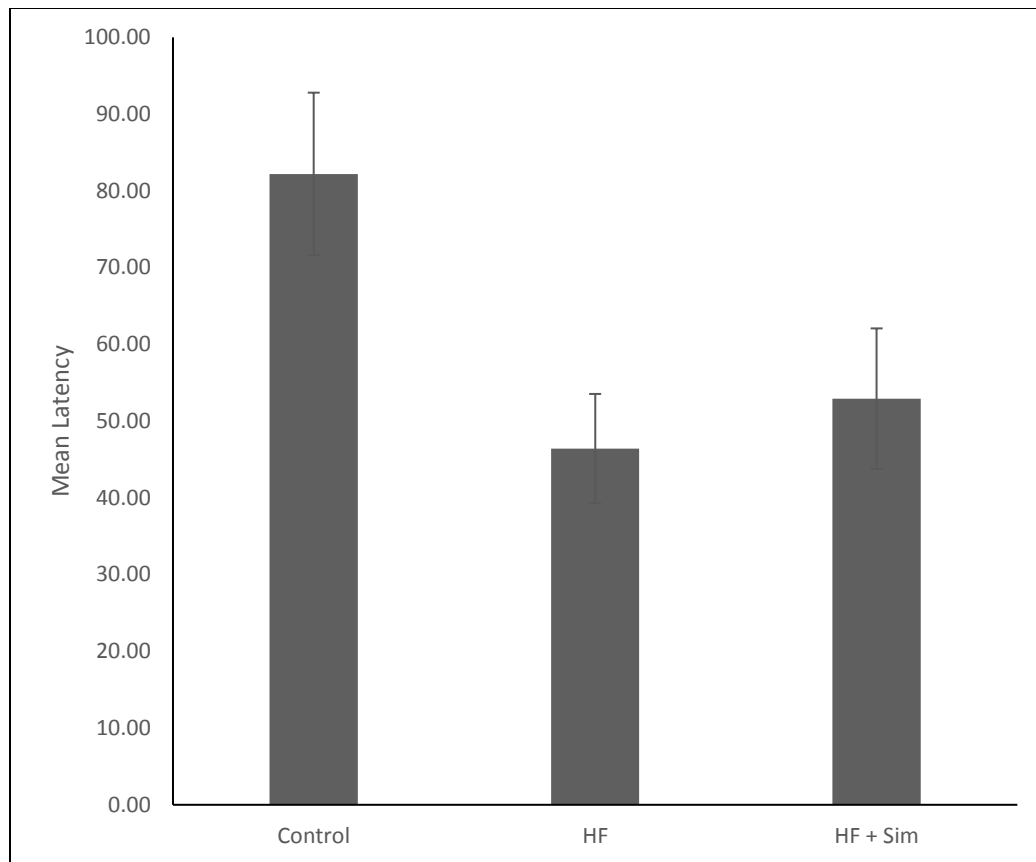| Groups	Sample Size	Treatment Duration (days)	Simvastatin Dosage per mouse (mg)	Avg. Mouse weigh (kg)	Avg. Total dosage per mouse (mg) / day
HF / Simvastatin	12	7	20	0.05	1.00
HF / Control	12	0	0	0.05	0
Untreated Control	12	0	0	0.035	0

Figure 1. Mean Rotarod latency across control, high-fat and high-fat treatment groups.
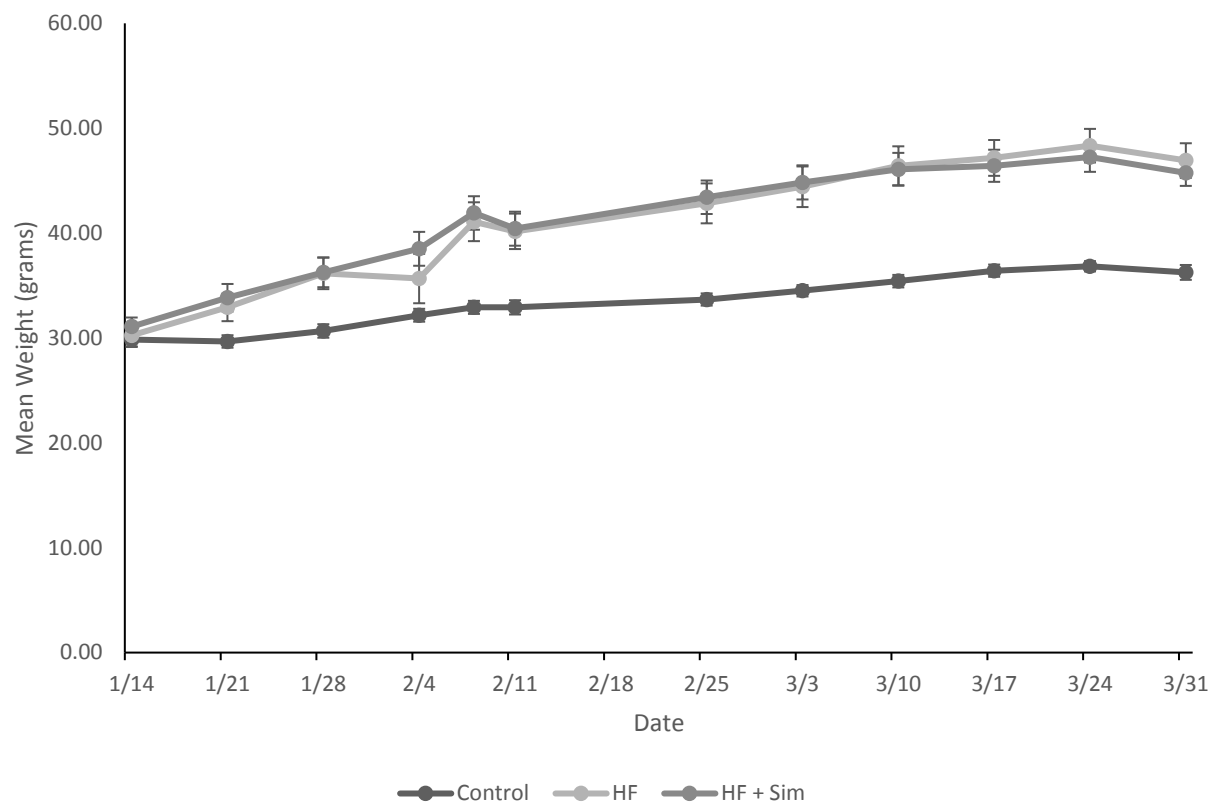
Error bars represent standard error.

Figure 2. Mean weight increase across groups over dietary period. Error bars represent standard error.
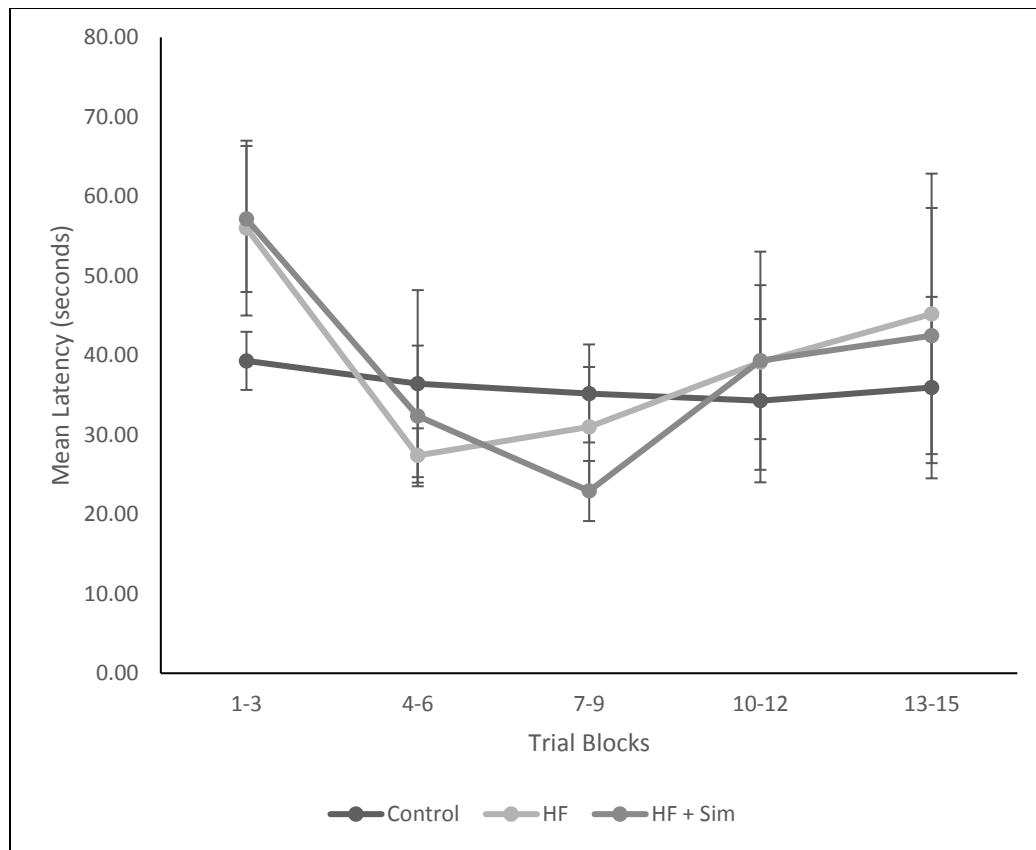
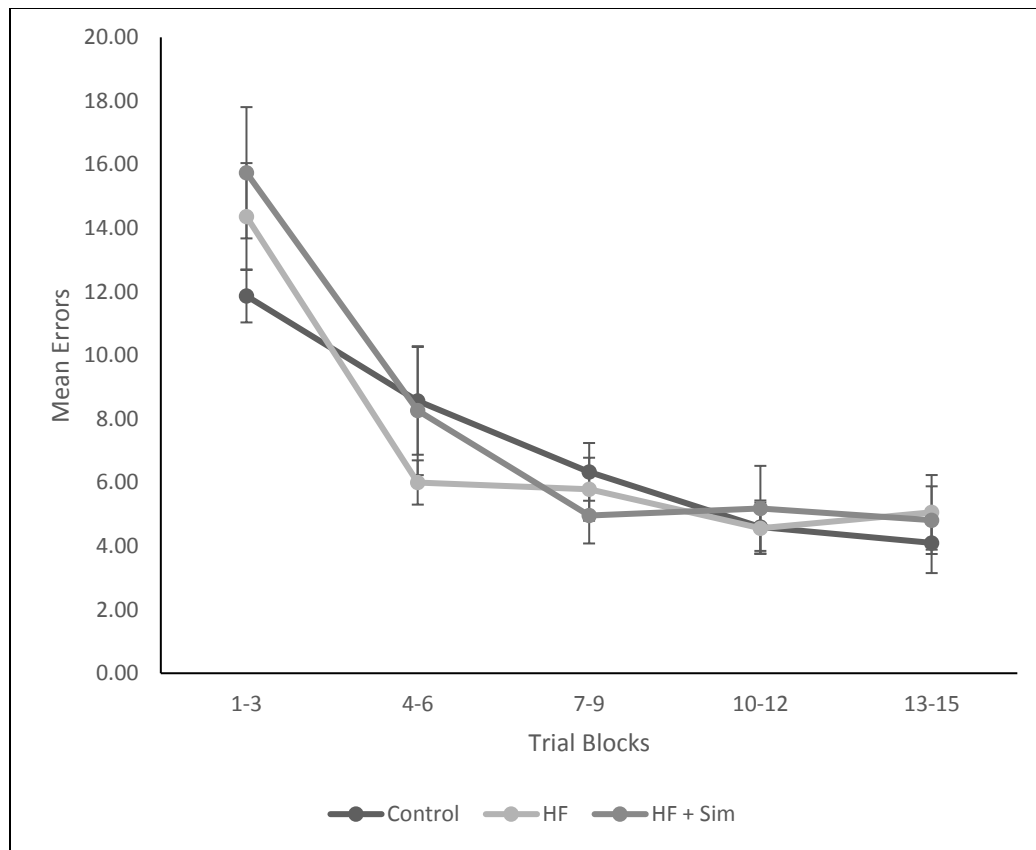*Figure 3.* Mean Stone T-Maze acquisition latency across groups. Error bars represent standard error.

Figure 4. Mean Stone T-Maze acquisition error rate across groups. Error bars represent standard error.

Appendix B: IACUC Protocol Approval

TOWSON
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December 18, 2015

Office of Sponsored
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Towson University
8000 York Road
Towson, MD 21252-0001

t. 410 704-2236
f. 410 704-4494

To: Paul Pistell, PhD

From: Towson University Institutional Animal Care and Use Committee
Louis DeTolla, Chairperson

RE: IACUC PROTOCOL# 12182015PP-02
Assessment of nutriceutical and pharmacological Interventions to
ameliorate experimentally-induced or natural age-related declines in
memory and motor function

This is to certify that the Institutional Animal Care and Use Committee has
reviewed your protocol and granted FULL APPROVAL.   The approval date
for this protocol is December 18, 2015

Your protocol is approved for a period of 3 years; an annual report must be
submitted to the IACUC six weeks before each anniversary date of the
protocol.

Please note your protocol will expire December 17, 2018.   If you need to
extend the protocol beyond this date, you must submit an Animal Care and Use
form at least three months prior to the expiration.

If you have any questions, please do not hesitate to contact the OSPR
Compliance Administrator by phone (410.704.2236) or email
(OSPR@towson.edu).

Louis DeTolla, VMD, MS, PhD, DACLAM
Chair and Veterinarian, Towson IACUC

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Christopher J. Wayman

To develop establish a professional position in the behavioral neuroscience and psychopharmacology research community.

Professional Accomplishments

Behavioral Neuroscience Research	**January 2014 - Present**

- CITI certified animal caregiver and researcher
- Specialization in diet and drug interventional research
- Highly controlled experimental environments
- Experience with intraperitoneal injection

Cognitive Neuroscience Research	**January 2014 – May 2015**

- Undergraduate psycholinguistic research exposure
- Conducting of experimental sessions and data collection
- Leadership, training and management of assistants

Teaching Assistant	**August 2014 – May 2015**

- Cognitive Psych, Psycholinguistics, Psychopharmacology
- Data entry and academic organization
- Acute attentiveness to student needs
- Interpersonal tutoring and conference

Meta-analysis of Psycholinguistic Literature	**November 2014 – May 2015**

- Critically analyzed range of N400 research
- Hybridization of data and analyses
- Repeat exposure to APA formatting and citation

Education

Master of Arts in Experimental Psychology	Towson University, Towson, MD	May 2017
		May 2015
Bachelor of Science in Psychology	Towson University, Towson, MD; 3.5 Cumulative GPA	
High School Degree	Fallston High School, Fallston, MD; 3.6 Cumulative GPA	June 2010

Employment History

Production Supervisor	Verb8tm - BTS Software Solutions, Towson, MD	December 2014 - Present
Coffee Master	Starbucks Coffee Company, Baltimore, MD	May 2012 – June 2014
Kitchen Expo, Chef	Bertucci's Italian Grille, Bel Air, MD	November 2009 – November 2011