Somato Publications ISSN: 2643-265X

Current Research in Neurology and Neurosurgery

Research Article

High-Fat Diet Reverses Neuroprotection Attained by Moderate Aerobic Exercise in the *Spastic* Han-Wistar Rat, a Model of Ataxia

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Received: 27 September 2021; Accepted: 16 October 2021; Published: 19 October 2021

Citation of this article: Younesi, S., Uhlendorf, TL., Lemus, AJJ., Ortega, BA., Gilhuys, MA., Olmos, M., Mitchell-Velasquez, EL., Perez, E., Jew, KL., Derkrikorian, N., Cohen, RW. (2021) High-Fat Diet Reverses Neuroprotection Attained by Moderate Aerobic Exercise in the Spastic Han-Wistar Rat, a Model of Ataxia. Curr Res Neurol Neurosurg, 4(1): 05-15.

Abstract

Diet and moderate exercise may promote effective therapies for patients with neurodegenerative diseases; however, administering a high-fat diet may exacerbate disease symptoms. To examine the effect of high-fat diet on exercise-induced neuroprotection, a high-fat diet was provided to *spastic* Han-Wistar (sHW) rats (*Rattus norvegicus*), a model of ataxia. Previously, we discovered that exercise led to improved motor activity and longevity, but not weight gain in the sHW mutant. What effect would a high-fat diet be on exercising mutants? Mutant and normal male siblings at 30 days of age were given either a high-fat diet (HF; 58% fat calories) or commercial rat chow diet (RC; 13% fat calories), and half of the rats were run on a treadmill at 15m/min for 30 min at a 15° incline for five days/week. While weight gain was similar among the exercising or sedentary mutants regardless of diet, a significant increase in longevity of the mutants feeding on the RC compared to the HF-fed mutants was observed. Normal rats were unaffected by consuming either diet. Brain-derived neurotrophic factor (BDNF) has been reported to be elevated after acute exercise. Hence, we investigated whether there was a correlation between the effect of HF treatment and BDNF expression quantified using an enzyme-linked immunosorbent assay (ELISA). Our results showed that BDNF levels in the cortex, hippocampus and cerebellum were affected by both diet and exercise ($p=0.009$). The benefits of this research could potentially aid in prescribing non-invasive dietary and exercise regimes for treating patients with neurodegenerative diseases.

Key Words: cerebellum, BDNF, ataxia, treadmill, Purkinje cells

Introduction

Cerebellar ataxia is a neurological motor disorder that includes loss of fine-motor skills and reduced cognitive ability [1]. Although ataxia can develop sporadically from non-genetic causes, ataxia mostly originates genetically. Autosomal recessive cerebellar ataxia (ARCA) forms include Wilson's Ataxia, Ataxia Telangiectasia, and the more common Friedreich's Ataxia [2]. In contrast, autosomal dominant hereditary ataxia types include Spinocerebellar Ataxia (SCA) that present motor dysfunction directly resulting from the progressive degeneration of Purkinje cells [3].

Currently, there is no cure for cerebellar ataxia, but there are multiple pharmaceutical and clinical procedures to combat this disease. Administration of certain drugs like Riluzole, Amantadine, and Varenicline has been shown to improve ataxic symptoms such as neuron excitability, depending on the type of ataxia [4,5]. Important to our study, exercise in the form of physical and occupational therapies has also been shown to provide a better quality of life for ataxic patients [6]. In animal models, moderate exercise regimens have been proven to be beneficial in slowing ataxia progression potentially through increases in antioxidant enzymes [7]. A previous study by Uhlendorf et al. [8] showed that moderate exercise enhanced neuroprotective properties within the cerebellum, leading to an increased lifespan in the *spastic* Han-Wistar (sHW) rat model of ataxia. In a subsequent study, Van Kummer and Cohen et al. [9] found that increased expression of Brain-derived neurotrophic factor (BDNF) and its receptor TrkB was correlated directly to exercise-induced neuroprotection in the sHW rat. Exercised rats for acute periods of time such as 7 days correlated with significant increases in BDNF though expression of BDNF was shown to decrease after chronic exercise (30 days).

Other than exercise, diet can also influence neurodegenerative disorders like ataxia. The negative consequences of a high-fat (HF) or high-caloric diet have been linked with cognitive impairment and neurodegeneration in the brain affected by increases in oxidative stress and neuroinflammation [10]. It has also been suggested that the cause of increased neuronal death in mice given a HF diet may be linked to an increase in lipid peroxidation [11]. The HF diet utilized in this particular study [11] also generated a significant decrease in neoneurogenesis in the dentate gyrus which was correlated with the decrease in BDNF because of malondialdehyde, a product of lipid peroxidation. In addition, HF diets have been shown to negatively affect the morphology and survival of neurons in male mice [12], leading to abrupt behavioral changes as well. Finally, it has been shown that a HF diet can influence epigenetics, such as DNA methylation in mice [13]. Together, these consequences of a high-fat diet can interfere with endogenous neuroprotection mechanisms.

For our study, we used the *spastic* Han-Wistar (sHW) rat, an animal model of cerebellar ataxia to investigate the effects of a high-fat diet on the progressive neurodegeneration of Purkinje cells. Previous studies with this sHW rat have revealed an unknown autosomal recessive mutation that conveys neurodegenerative abnormalities in the cerebellum displaying progressive degeneration of Purkinje cells [14-16]. In previous studies, Purkinje cell loss was attributed to being in a continuously excited state - this glutamate excitotoxicity was confirmed by the blocking of *N*-methyl-D-aspartic acid (NMDA) receptors [17] and non-NMDA receptors [18] which extended the lifespan of the mutants significantly. Primary symptoms associated with the sHW rat include hyperactivity and slight forelimb tremors visible at about three weeks postnatal [15]. By six weeks, the sHW mutant is visibly different from its normal littermates. The foot placement is clumsy and unsynchronized, similar to ataxic patients. Complete loss of hind limb motor coordination occurs around 60-65 days followed by death a few days after.

However, if sHW mutants were exercised chronically, symptoms were ameliorated significantly; but ataxic progression was still present, and these exercised rats lost weight more than sedentary mutant littermates [8]. But what happens if these mutant sHW rats were given a high-caloric diet (in the guise of high-fat content) to increase their weight? Although previous studies looked at similar diseases and the role of BDNF, we posit here that diet and exercise can also play a broader, but still important inter-related role. We would therefore hypothesize this high-fat diet might affect exercise-induced neuroprotection by extending longevity. This current study examined the long-term effects of a high-fat diet on the longevity, motor behavior and BDNF levels of these sHW rats subjected to chronic, moderate exercise.

Materials and Methods

Animals

All animals were obtained from the breeding colony located at California State University, Northridge. Young sHW mutant and normal male littermates (approximately 30 days old) were used in the study. We opted to use only male rats in this study for two, unrelated reasons: 1. Since we linked this current study with our previous published experiments [8,9] that tested male mutants solely, to make all comparisons relevant, we only used male rats here as well; 2. Because of the possible neural effects of estrogen, which has been shown to influence the weight, locomotor activity, and possibly longevity [19], we decided on an all-male rat comparison study.

All rats were housed in standard cages and had free access to water and either LabDiet 5001 rodent chow (RC diet; 13.4% kcal fat, Purina) or high-fat diet (HF diet; 58% kcal fat, Research Diets, Inc Surwit D12330). Experiments began when the animal reached 30 days of age. The cages were kept at 22.2±1°C and a 12-hour light/dark cycle in the CSUN vivarium. All experimental protocols in this study were approved by CSUN's Institutional Animal Care and Use Committee (Protocol #0809-011b).

High-Fat Diet Experiments on sHW Mutant Weight Gain

The first diet experiment utilized the HF diet or RC diet on sHW mutant and normal male sibling controls to determine if there were any differences in weight gain. At 30 days old, male mutant and normal sibling pairs were randomly divided into either high-fat (HF) or regular rat chow (RC) groups (mHF n=10, nHF n=10, mRC n=8, nRC n=8). All rat groups had free access to either HF or RC diet until the experiment ended when the mutants died, typically around 65 days of age. Each animal's weight was an assessment of health and was recorded every five days.

High-Fat Diet and Moderate Exercise Experiments on sHW Mutants

The second diet-exercise experiment used only mutant male sHW rats which were randomly divided into treatment groups to compare high-fat (HF) and rat chow (RC) diet groups, and then further divided into runner (R) and non-runner (NR) groups (HF-R n=10, HF-NR n=10, RC-R n=12, RC-NR n=8). As an assessment of health, weight, and two motor assays were taken every five days on all animals. Monitoring was recorded over the lifespan of the rats and included the evaluation of longevity.

The moderate aerobic exercise treatments were conducted on a motorized treadmill (Columbus Instruments Treadmill 3R) to examine the effects of HF or RC diet consumption in mutant rats that exercised chronically. At 30 days of age, sHW male mutants ("runner" group) were placed on the treadmill for 30-minute sessions. All treadmill experiments conditions were as followed: speed was set at 15 meters/minute at a 15° incline that was lowered with the progressively diminished physical capabilities of the sHW mutants. The sedentary rat group ("non-runner" group) was brought into the treadmill room but stayed in their enclosures. All animals were run 7 days a week until mutants could no longer run.

Motor Activity Experiments on sHW Mutants

To quantify the any observed decrease in locomotor activity, we used open-field testing. Animals were tested in an open-field arena just prior to treadmill exercise using a 36cm×55cm×18.5cm plastic bin divided into fifteen, 10cm×10cm squares. The test consisted of three, non-consecutive trials, each lasting two minutes with 30 seconds allocated for rest between trials. A motor activity point was given each time the rat either crossed a square or reared up. Total motor activity points in each trial were averaged, and a net motor activity score was determined for that time point. The initial tests were performed on their first day of running (30 days of age) and then every 5 days until 60 days of age when many of the mutants could no longer perform the activity.

BDNF Analysis

To quantify the expression of BDNF in a short term (seven days) experiment of diet and exercise was utilized. For this study, we used mutant male sHW rats (mHF-R n=6, mHF-NR n=6, mRC-R n=6, mRC-NR n=6) and additional normal male siblings (nHF-R n=6, nHF-NR n=6, nRC-R n=6, nRC-NR n=6). For this biochemical analysis, we started exercising all rats at 30 days. Seven days after initiating daily treadmill exercise treatment (30 min running, 15 meters/min, 15° incline) the cerebellum, hippocampus, and cortex were extracted, weighed, frozen on dry ice, and stored at -80°C until quantification with a BDNF sandwich enzyme immunoassay (ChemiKine™ Sandwich ELISA kit, CYT 306, Millipore). The 50 mg tissue samples were homogenized with 1 mL of ice-cold buffer: 100mM Tris/HCl, 2% BSA, 1M NaCl, 4mM sodium EDTA, 2% Triton X-100, 0.1% sodium azide, and protease inhibitors 5µg/ml aprotinin, 0.5µg/ml antipain, 157µg/ml benzamidine, 0.1µg/ml pepstain A, 17µg/ml phenylmethyl-sulphonyl fluoride via sonication (Fisher Scientific, Model 100 Ultrasonic Dismembrator). The samples were then centrifuged at 14,000 RPM for 30 min, and the samples were diluted 1:2 with the kit's sample diluent and added to the ELISA 96-well plate which was pre-coated with murine anti-Human BDNF monoclonal capture antibody. The plates were incubated on a shaker overnight at 4°C. After overnight incubation, well contents were washed four times with 250µL of wash buffer. To detect the captured BDNF, 100 µL of biotinylated mouse anti-BDNF monoclonal antibody (1:1000) was added to each well and incubated on a shaker at room temperature for 3 hours and then well contents were washed four times. 100µL of streptavidin-HRP enzyme conjugate (1:1000) was then added to the plates and incubated at room temperature for one hour then washed four times again. 100µL of TMB/E substrate was added to each well, and the plates were incubated at room temperature for 15 minutes after which 100µL of stop solution (0.1N HCl) was added to each well. Plates were read immediately using a spectrophotometer microwell plate reader (Spectra MAX 190) at 450nm using SoftMax Pro 5.4.1 software. To determine the concentration of BDNF in the well plates, absorbance readings were given as optical density (OD) values and then converted into concentrations (pg/mL) based on BDNF standards. Samples were normalized by converting the BDNF values to pg/mg wet weight of tissue.

Statistical Analysis

Multiple comparisons for the weights, activity test, and longevity were analyzed by one-way analysis of variance (ANOVA) for individual groups. Weights and activity test were additionally referenced with Repeated Measure ANOVA. In the longevity experiment, the significant differences were determined by *t*-test. For the BDNF experiment, since the variances were similar, the significant differences were determined by the two-way ANOVA for multiple groups, three-way ANOVA for cross determining any interaction effects. Post-hoc analysis was done using Tukey's HSD tests. Figures were generated using Excel, and for BDNF analysis, GraphPad Prism 5 software and data analysis were done using R Studio software. All values are expressed as mean±SE, and $p<0.05$ was considered statistically signifi-

cant.

Results

Effects of a High-Fat Diet on sHW Weight Gain

To investigate whether or not a high-fat (HF) diet would have any effect on sHW mutant rats, we compared the weights of mutants and normal rats feeding on either HF or rat chow (RC) diet (Figure 1). We found that regardless of consuming HF or RC diet, there was a steady and non-significant increase in mass until 60 days of age by mutant sHW rats (Repeated Measure ANOVA; $F=0.683$, $p>0.05$). Normal littermates weighed the same regardless of HF or RC diet groups, showing no significant difference. As expected, there was statistical significance between mutant and normal control weights regardless of diet (Repeated Measure ANOVA; $F=81.93$, $p<0.001$).

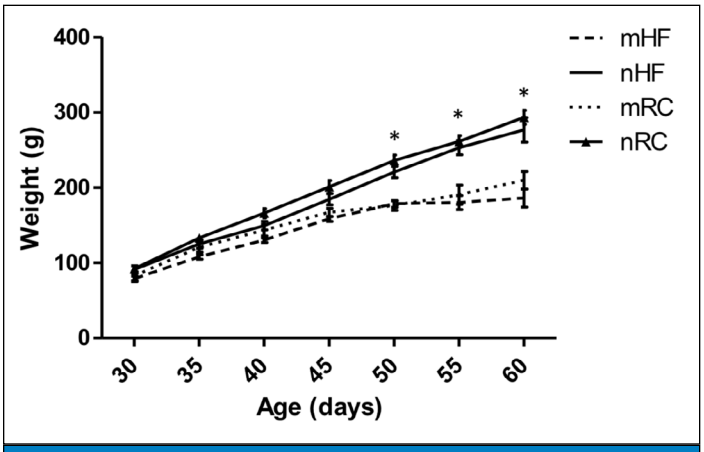

Figure 1: Mean weights of normal and mutant sHW rats fed either high-fat (HF) diet [nHF (n=10) and mHF (n=10)] or rat chow (RC) [nRC (n=8) and mRC (n=8)] starting at 30 days of age. Normal rats weighed approximately the same regardless of HF or RC diets, showing no significant difference. However, mutants showed substantially less weight gain compared with normal controls after 45 days, showing overall significance between mutant and normal weights regardless of treatment ($F=81.93$; $p<0.0001$). Finally, there were no significant differences between HF and RC mutant weights at any age range ($F=0.683$; $p>0.05$). Asterisks mark significant differences between normal and mutant groups. All values are means ± SEM.

Effects of High-Fat Diet and Exercise on sHW Mutant Weight Gain

To examine whether or not moderate exercise and diet had any effect on the sHW mutants, we compared the weights as an assessment of health for five days a week until 60 days of age (Figure 2). As expected, mutant weight increased from 30 days until 50 days old, and plateaued at 55 days of age; with the exception of RC-NR which showed a small, insignificant drop in weight gain at 60 days of age. Although there was a weekly effect of animal weight over the length of the experiment (Repeated Measure ANOVA, $F=27.40$; $p<0.005$), there were no statistical differences among any mutant group with exercise regardless of diet.

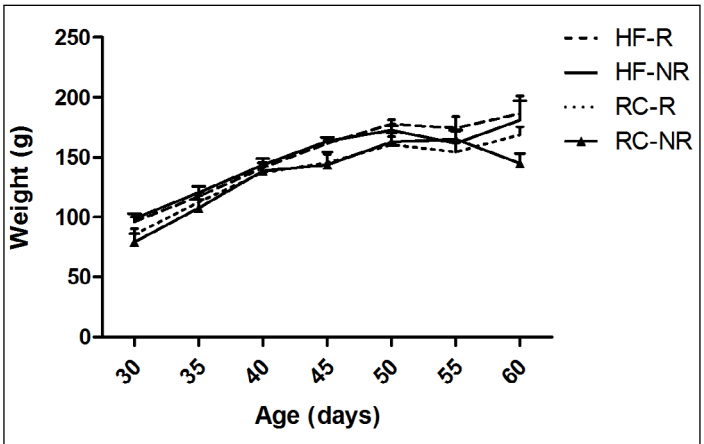

Figure 2: Mean weights of mutant sHW runners and non-runners feeding on either high fat or rat chow diets [HF-R (n=10), HF-NR (n=10), RC-R (n=12), RC-NR (n=8)] starting at 30 days of age. Although there was an effect on animal weight over the length of the experiment ($F=27.40$; $p<0.05$), there were no statistical differences among any mutant group with exercise regardless of diet. All values are means ± SEM.

Motor Activity Scores on Exercised sHW Mutants

To examine if the treadmill running had any beneficial effects on the ataxic symptoms of the mutant sHW rat, an assessment of the locomotor activity level was taken every five days until 60 days of age (Figure 3). Motor activity scores between the mutant HF or RC diets regardless of exercise regime showed no significant differences (Figure 3), with both declining in activity at the same rate. The nor-

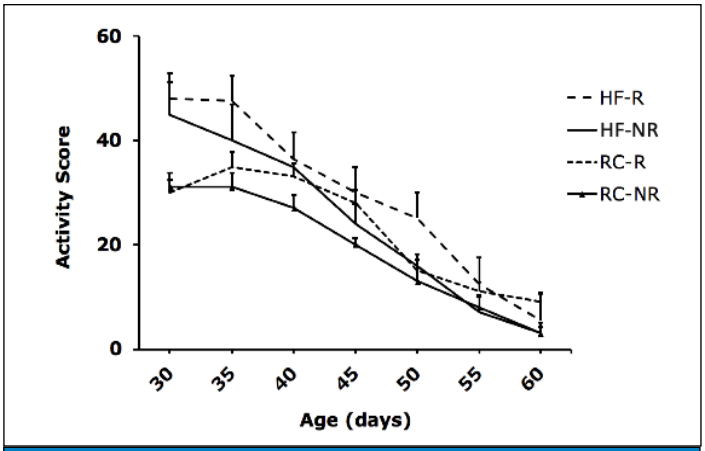

Figure 3: Mean motor activity levels of mutant sHW animals fed either high-fat (HF) diets or rat chow (RC) [HF-R (n=10), HF-NR (n=10), RC-R (n=12), RC-NR (n=8)] starting at 30 days of age. Motor activity was analyzed with Repeated Measure ANOVA that showed significance as all mutants aged (F=397.61, p<0.0001) and was consistent with the observed progressive decline in motor activity observed in the sHW mutant. Values are means ± SEM.

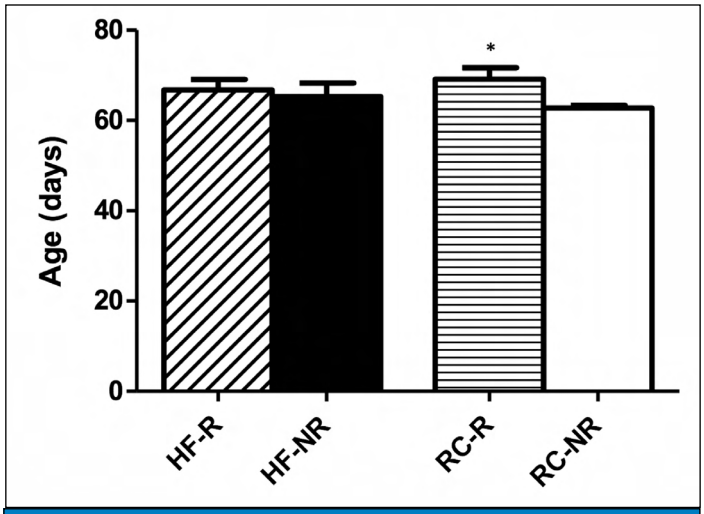

Figure 4: Mean longevity of mutant sHW animals fed either high-fat (HF) diets or rat chow (RC) [HF-R (n=10), HF-NR (n=10), RC-R (n=12), RC-NR (n=8)]. In the rat chow group. there was a significant 12.2% increase comparing runners to sedentary mutants (t=2.36, p=0.04). In contrast, there was a non-significant 4.9% increase in longevity (paired t-test: t=0.39, p=0.74) in the HF-R group compared to the HF-NR. Asterisks mark significant differences between mutant rat chow runners versus rat chow sedentary group. All values are means ± SEM.

mal animals on HF or RC diets regardless of exercise were constant in their motor activities throughout the experiment with no significant differences among these groups (data not shown). Repeated Measure ANOVA showed significant effects within age (F=397.61; p<0.001), and is consistent with the observed progressive decline in motor activity in mutant sHW rats.

Longevity of sHW Mutants fed HF diets

Mutant sHW rats fed control diet (rat chow) that were exercised exhibited less severe ataxic symptoms (Figure 4) and lived statistically longer than their sedentary counterparts (12.18% increase in RC-R to RC-NR; paired t-test: t=2.36, p=0.04). In comparison, there was no significant difference in longevity between the exercised and sedentary high-fat diet groups (paired t-test: t=0.39, p=0.74).

BDNF Levels

We investigated whether BDNF levels were correlated to high-fat diet and exercise, in the seven-consecutive day acute exercise regimen. Here, the mutant and normal sHW rats were HF-R (n=6), HF-NR (n=6), RC-R (n=6), and RC-NR (n=6) were given either a high-fat diet or regular rodent chow and either exercised or non-exercised for seven consecutive days before brains were removed for BDNF analysis using sandwich ELISA kit (Figure 5). When comparing normal rats to mutant rats, there was a significant decrease in the concentration of BDNF in mutant rats compared to normal rats (F=15.84, p=0.00012). When the HF diet was compared to RC diet there was a significant decrease in BDNF for rats that consumed HF diet compared to the RC diet (F=72.32, p<0.005). Within specific brain regions there was also significantly higher in BDNF levels in the cerebellum and hippocampus compared to the cortex (F=252.80; p<0.001). There was also a significant combined effect of diet and phenotype (F=9.23, p<0.02), diet and brain part (F=18.50, p<0.01), also phenotype and brain part (F=30.39, p<0.001), and exercise and brain part (F=4.33, p<0.02) and exercise, phenotype, and brain region (F=5.46; p<0.02).

Discussion

In summary, we aimed to establish the beneficial effects of a high-fat (HF) diet and moderate exercise on ataxia utilizing the *spastic* Han-Wistar (sHW) rat model. However, coadministeration of high-fat diets during either acute or chronic, moderate exercise regimens to the sHW mutants showed substantial deleterious effects, reversing positive trophic outcomes that we previously observed from exercising these mutants [8, 9]. These exercise-induced positive results included increased longevity, reduced Purkinje cell death [8], and an increase in BDNF in the cerebellums of exercised mutants [9].

In our present experiment, mutant longevity was affected by HF diet treatment, statistically similar for this mutant treatment groups. In contrast, exercised mutants on rat chow lived 12% longer than sedentary control mutants. Interestingly, observed a similar and significant increase in longevity (14%) of excercised mutants in their earlier study [8]. Yet, weight gain was not affected by diet and only differed between mutant and normal groups (a result observed in all of our lab's previous publications regardless of diet). Motor activity levels (Figure 3) did differ significantly especially as the mutants aged, reflecting the progressive severity of ataxic symptoms. Mutants that exercised retained some motor activity function than their sedentary counterparts and were still able to run on the treadmill despite the late progression of the disease. Our lab has previously shown that acute exercise increases the BDNF levels of the sHW, potentially conveying neuroprotective effects via BDNF [9]; here, mutant rats consuming a HF diet failed to display these BDNF enhancements. Our conclusion: a high-fat diet diminished this BDNF-directed improvements in motor ability and longevity in the sHW rat.

One possible reason for the lack of exercise-enhanced improvements in high fat fed mutants is experiment time. Our experiment lasted until the mutant perished (approximately 65 days) about 30-35 days after onset of any diet or exercise treatment. Treadmill running did elicit some minor, yet non-significant improvements to the sHW rat. In contrast, other related studies used a obese rat model for at least eight weeks [20], and thus, longer duration of exercise combined with diet could very well be a correlating factor. In fact, relevant studies on mice regularly exceeded four weeks of treatment with differences appearing at 6-8 weeks and lasted 15 months, suggesting that a longer duration could potentially reveal motor differences [11]. Yes, it may take longer for some physiological responses to be significantly noticable, but due to the limited life-span (approximately 65 days) of the sHW rats, these chronic exercised-induced improvements may not have become evident.

A high-fat diet should also have an effect on the rate of weight gain. Although Sprague-Dawley rats on this specific diet gained weight rapidly, usually within one or two weeks [21], our Han-Wistar rat strain did not. It may be possible that this particular strain of sHW rats may be resistant to rapid weight gain when feeding on a high-fat diet. Studies have shown that Wistar rat strain requires chronic feeding on a HF diet for a significantly longer term (at least 12 weeks) to induce an obese phenotype [22]. Another experiment using Han-Wistar rats and a high-fat diet regime showed first significance at the sixth week [23]. In our experiment, we used the Surwit 58% kcal diet to represent a diet high in saturated fats mainly from hydrogenated coconut oil. Although it is usually recommended to avoid saturated fats in human diets, saturated fats are not necessarily the cause of diseases such as diabetes, stroke, heart diseases or obesity [24]. The increase of free fatty acids has been shown to lead to an increase of lipid peroxidation in the brain, exacerbating neurodegeneration [25]. We therefore hypothesized that in the sHW rat strain we would expect to see an exacerbation of the ataxic symptoms, but this was not observed. Thus, the answer to this enigmatic result must lie elsewhere. We suspect that the culprit was BDNF expression.

BDNF plays an important role in nerve cell survival and is implicated in neurogenesis in multiple regions of the

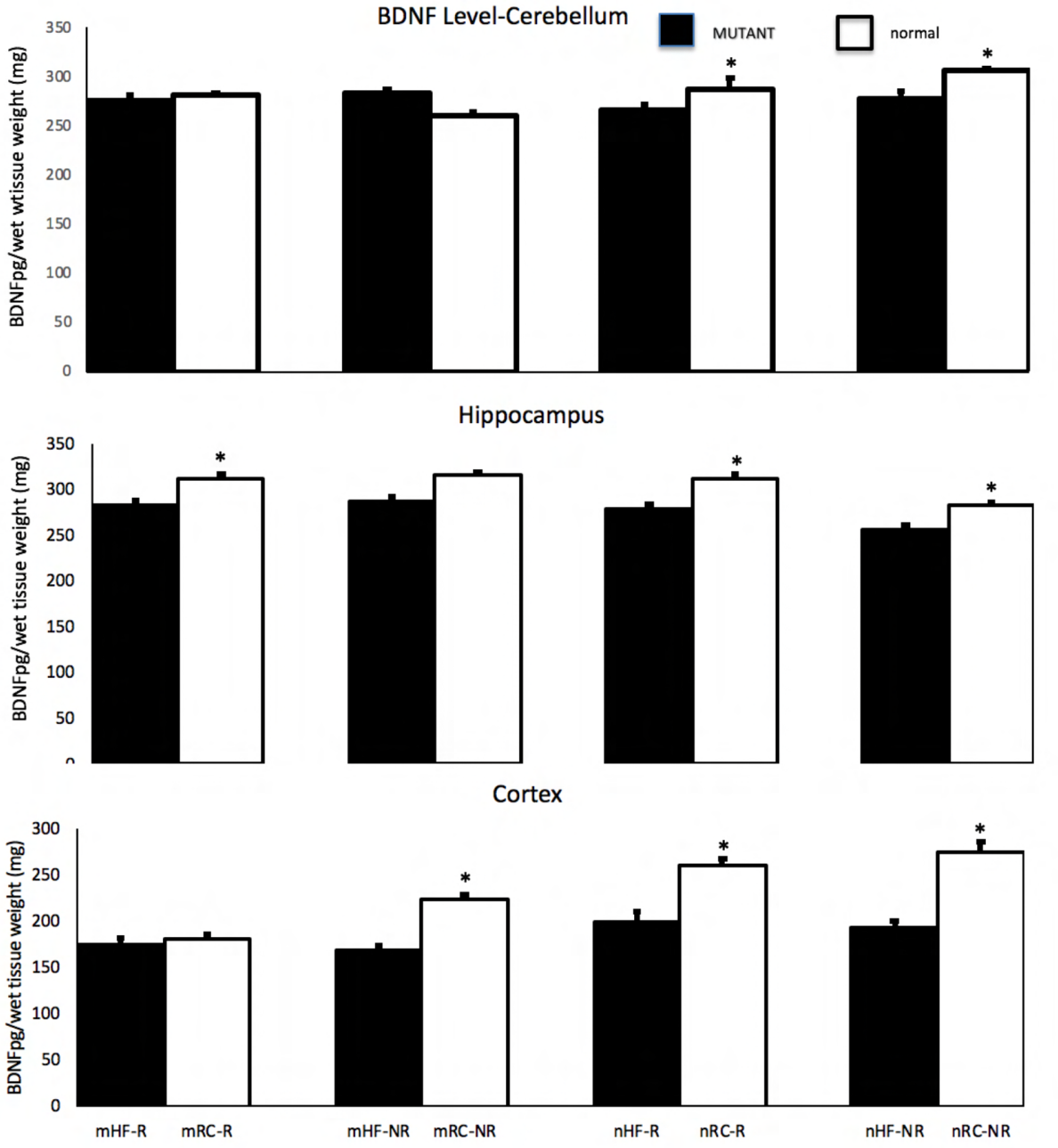

Figure 5: BDNF concentration (pg/mg wet weight of tissue) from the cerebellum, cortex, and hippocampus (HF-R, n=6; HF-NR, n=6; RC-R, n=6; RC-NR, n=6) for both the mutants and the normal rat groups either exercised or sedentary. There was a significant decrease in the concentration of BDNF in mutant rats compared to normal rats (F=15.84, p=0.012e-2). Overall high fat groups displayed significantly lower BDNF levels compared to the regular chow rats regardless of exercise treatment (F=72.32, p=0.05e-16) with the exception of cerebellar mHF-NR. Within specific brain regions there was also significantly higher in BDNF levels in the cerebellum and hippocampus compared to the cortex (F=252.80; p=0.001e-16). There was also a significant combined effect of diet and phenotype (F=9.23, p=0.002), diet and brain part (F=18.50, p=0.009e-10), also phenotype and brain part (F=30.39, p=0.002e-13), and exercise and brain part (F=4.33, p=0.015) and exercise, phenotype, and brain region (F=5.46; p=0.005). Asterisks mark significant differences between normal and mutant groups. All values are means ± SEM.

brain [11,26]. BDNF has been shown to activate different pathways, including the JAK/STAT pathway, causing the release of cytokines that promote nerve regeneration [27]. BDNF is also a modulator of inhibitory synapses where it acts via TrkB receptors [9]. It has been suggested that BDNF mRNA in cerebellar ataxias is expressed at low levels, but BDNF protein becomes localized in elevated levels within dendritic branches [28]. In our rat model, Purkinje and granule cells may be protected from stress-induced apoptosis by BDNF [29]. Mechanistically, this has been shown to be accomplished by maintaining synergistic dendritic branching and synaptic activity with neighboring glial cells (i.e., microglia and astrocytes) that increase BDNF activity [30,31]. This increase in cell-cell activity, and ensuing BDNF activity could be what promotes cell survival. In another experiment with the ataxic stargazer mouse, it was shown that a faulty expression of BDNF led directly to cell death in the cerebellum [32]. Previous work done by our lab has correlated progressive Purkinje death with the severity of ataxic symptoms of the sHW rat [8, 9].

Though the exact mechanism with which a HF diet affects BDNF expression is not precisely clear, there are many possible methods. It is known that BDNF can act as a regulator of vesicle transport at the neuronal synapse, and it has been suggested that HF-induced obesity causes decreases in BDNF protein and pro-BDNF levels due to cellular stress in the hippocampal endoplasmic reticulum [33]. This observation was reversed when rats were subjected to aerobic exercise that could explain the differences in our experiment between HF-R and HF-NR BDNF levels. A similar study found that HF diet can lead to increased levels of oxidative stress that disrupted normal levels of BDNF [20] perhaps revealing why we observed lower levels of BDNF in the HF animals, with the one exception in the cerebellum. In our current experiment, overall the BDNF levels were unusually lower in brains of rats feeding on the HF diet compared to their RC control groups. These differences could be due to the metabolic breakdown of HF diet, releasing reactive oxygen species (ROS) that damage neurons [11]. Previous work has shown BDNF has neuroprotective effects by preventing cell death in the mouse brain triggered by lipid peroxidation from HF diet [11].

Conclusion

The aim of our study was to investigate whether or not a high-fat diet during an acute exercise regimen would have an effect on the phenotype of the *spastic* Han Wistar rat, a model of ataxia. We found that longevity was significantly reduced by any exercise with high-fat treatment. To accelerate weight gain, future studies will take advantage of diet-induced obesity specialized rat chow. This can potentially overcome the difficulty of developing an obese sHW ataxic model. In terms of human medicine, new medications and medical procedures have been shown to be very beneficial in treating patients suffering from neurodegenerative disorders. In this study, we offer new evidence that lifestyle changes involving reduced fat diets should be utilized as a vital part of any treatment plan to prevent and treat neurological diseases.

Acknowledgements

The authors want to thank Brandon D. Griess for his support in gathering data, and to Jesse Magaña, and Kate Tirado-Gonzalez for long-term care of the animals in the vivarium.

Conflict of Interest Statement

The authors have no conflict of interest to declare.

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