SURVEY OF BRAIN VARIATIONS OF YOUNG ADULT AND AGED β2 (-/-) KNOCKOUT MICE

A Senior Honors Thesis

by

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ABSTRACT

Survey of Brain Variations in Young Adult and Aged β2 (-/-) Knockout Mice (April 2008)

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Neuronal nicotinic acetylcholine receptors (nAChRs) are pentameric, ligand-gated ion channels whose activation is triggered by the neurotransmitter acetylcholine and by the exogenous compound, nicotine. In previous studies, disruptions in high affinity nAChR function have been shown to contribute to neuronal dysfunction as observed in Alzheimer's disease (AD), Parkinson's disease (PD), Lewy body dementia, autism, epilepsy, and schizophrenia. To study the effect of nAChRs, knockout mice, or mice genetically altered to lack certain subunits of their nAChRs, have been created. β2 (-/-) knockout mice lack the β2 subunit of their nicotinic acetylcholine receptors. These β2 (-/-) knockout mice have been shown to have a shorter lifespan, altered brain development and altered CNS function similar to changes seen in human ageing, making

them a useful animal model for human dementia and neurodegeneration. It has been hypothesized that the β2 subunit has neuroprotective properties with respect to the neurons that express nicotinic acetylcholine receptors.

The purpose of this study is to compare the volumes and cell densities of the olfactory bulb and the hippocampus in young adult (2-3 month old) and aged (18 month old) male β2 (-/-) knockout mice and age-matched wild type (+/+) mice. Both the olfactory bulb and hippocampus exhibit adult neurogenesis and the hippocampus is an important center for spatial learning and memory. We hypothesized that mice lacking the β2 subunit of their nAChRs, have excessive cell loss and therefore decreased brain area and that this effect would be pronounced in older β2 (-/-) knockout mice compared to younger mice. Currently, young adult mice (2-3 month old), have been evaluated, and no significant statistical difference in the olfactory bulb volume or hippocampus volume in β2(-/-) knockout mice compared to age-matched control mice has been observed. The olfactory bulb granular cell layer density of 2-3 month old mice also showed no significant difference compared to age-matched control mice. In aged mice (18 months old), hippocampus volumes and olfactory bulb volumes were measured and found to be the same as observed in the age-matched wild type group. In the future, cell densities of hippocampus in young adult mice and cell densities of olfactory bulb and hippocampus of aged mice, should be studied.

DEDICATION

I would like to dedicate this thesis to my uncle, Dr. Joe Kuban, who was diagnosed in the fall of 2006 with the neurodegenerative disease, Amyotrophic Lateral Sclerosis (ALS), often referred to as "Lou Gehrig's disease." His love for research and his struggles throughout his disease has influenced me to take on my Fellows research in the field of Neurodegeneration. Keep Truckin' Uncle Joe!

ACKNOWLEDGEMENTS

First and foremost, I would like to thank Dr. Louise C. Abbott for all of her support and belief in me. There were times of struggle, but she was always there to push me and keep me going. My Fellows experience would not have been possible without her. She took me under her wing and taught me many lessons, both in the lab and out, and for that I am very grateful. Thank you doesn't say enough.

Secondly, I would like to thank Pei-San Huang for her constant guidance and help throughout my project. Her knowledge and work in sectioning and staining have been invaluable to me. This project would not have been possible without her. Thank you for you patience in explaining and re-explaining details to me even though I was always sure I had it the first time around!

Third, I must thank my parents, John and Becky Kuban. Their constant support has always kept me going. Mom, thanks for always making sure I take deep breaths, reminding me that life goes on and I should eat dinner. Many times I would have forgotten! Dad, Thanks so much for showing your support by coming to Student Research Week and always indulging in my "big-word" scientific conversations at Agave.

Finally, I would like to thank my research friends, Emily Murawski, Asher Schusterman, Matt Propst and Ransom Wise. Having you in the lab has always brightened my day! Thanks for all of your support! Special thanks go to Matt for answering my late-night panicky phone calls and being my fellows meeting sidekick.

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INTRODUCTION[1]

Overview

Over the past decade, the focus on neuronal nicotinic acetylcholine receptors and their subunits have been a hot topic of research in the field of neurodegeneration. With the development of transgenic mice specially modified to express or not express certain subunits, researchers can better understand the underlying mechanisms by which certain neurodegenerative diseases occur. The topic of this study, β2 (-/-) knockout mice, have proven useful in studies of Alzheimer's disease, Parkinson's disease, and other neurodegenerative disorders.

Many studies have focused on the cognitive functionality of these β2 (-/-) mice, including learning, memory and attention (Marubio and Changeux, 2000). Few studies, however have surveyed the morphological differences that may occur in different brain regions between β2 (-/-) mice and age matched control wild-type mice.

Nicotinic Acetylcholine Receptors

Nicotinic acetylcholine receptors (nAChRs) have roles in development and synaptic plasticity, and nicotinic mechanisms play a part in attention, memory and learning (Dani and Bertrand, 2007). Modifications or alterations of these mechanisms can contribute to the dysfunctions of common neurological disorders, such as epilepsy, schizophrenia, Parkinson's disease, autism, dementia with Lewy bodies, Alzheimer's disease, and addiction (Dani & Bertrand, 2007).

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[1] This thesis follows the style and format of the *Journal of Neuroscience.*

nAChRs are expressed in many regions of the central nervous system (CNS) and peripheral nervous system (PNS) (Cordero-Erausquin et al., 2000). The focus of this study is nAChRs expressed in the CNS or neuronal nAChRs. From herein, nAChRs discussed will be assumed to be neuronal. Structurally, nAChRs are pentameric ligand-gated ion channels whose opening is triggered by the neurotransmitter, acetylcholine, and the exogenous chemical, nicotine. In mice, nAChRs can consist of combinations of six α (α 2-7) and three β (β 2-4) subunits (Cordero-Erausquin et al., 2000). These subunits associate in combination to form functional homopentamers, which are pentamers consisting of only one type of subunit (usually α 7, α 8, or α 9), or heteropentamers, which are commonly found in combinations of two α and three β subunits (Rossi et al., 2001). Two groups of nAChRs have been identified based on their high affinity for binding either nicotine or α –bungarotoxin. The former are considered to be formed by α 4- and β2-subunit-containing nAChRs and the latter are thought to be α7 containing nAChRs (Cordero-Erausquin, 2000).

Nicotine and Neuroprotection

Nicotine acts like a neurotransmitter with respect to nAChRs by binding with the receptor and stimulating it as acetylcholine would when it is normally released from the pre-synaptic terminal in typical synaptic transmission. An increased uptake of nicotine into the CNS has been shown to stimulate cholinergic systems throughout the brain. In turn, stimulation of the cholinergic system has been associated with the release of the neurotransmitters dopamine, an important neurotransmitter in reward mechanisms, and

glutamate, which is important in memory and learning (Drago et al., 2003). These revelations led to the idea of a relationship between activation of nAChRs and maintenance of cognition in aging and dementia. Furthermore, studies have shown a loss of cholinergic markers, including nicotine binding sites and nAChR subunit expression, in human subjects with many types of dementia (Picciotto and Zoli, 2002). Loss of nAChRs is correlated with a reduction of cholinergic function that could contribute to the cognitive deficits associated with dementia (Picciotto and Zoli, 2002). To further this idea, in an epidemiological review, Fratiglioni and Wang (2000) suggested that chronic increased levels of nicotine, as observed in smoking or use of other tobacco products, may be protective against the development of neurodegenerative diseases such as Alzheimer's disease (AD) or Parkinson's disease (PD).The review proposed that nonsmokers have approximately twice the risk for developing AD or PD than smokers (Fratiglioni and Wang, 2000). This observation suggests that increased chronic nicotine exposure may be correlated with a neuroprotective effect on the cholinergic system by either slowing the progression of neurodegeneration, increasing cell proliferation, or improving cognitive abilities in patients with neurodegenerative diseases.

B2 (-/-) Knockout Mice

To study neuroprotective effects, research has been aided by the used of transgenic mice, or mice genetically altered to lack individual nAChR subunits, such as the β2 (-/-) knockout mice used in this study. As mentioned previously, the β2 subunit of nAChRs is considered to be a high affinity nicotine binding receptor and is present in heteropentamers of nAChRs of β2 (-/-) knockout mice. The β2 subunit was one of the

first nAChR subunits targeted in knockout experiments (Drago et al., 2003). β2 (-/-) mice are particularly important because they lack the high affinity binding of nicotine that has been shown in epidemiological studies to be beneficial in the previously described neurodegenerative diseases (Drago et al., 2003). Furthermore, β2 knockout mice have anatomical and behavioral deficits similar to pathological aging; therefore, these mice serve as a useful model for the study of dementias (Marubio and Changeux, 2000) as well as neuronal health during normal aging (Zoli et al., 1999).

Behavioral Deficits

The first publication on β2 knockout mice by Piciotto and Zoli in 1995, suggested that the β2 nAChR subunit is required for nicotine-mediated improvement of passive avoidance, a paradigm that is thought to mimic memory and learning functions in mice (Drago et al., 2003). In the experiment described by Drago et al. (2003), latency of a mouse to perform a task for which it has already been punished for, in this case, entering a dark chamber was tested. B2 knockout mice showed a higher latency for the punished action therefore implying a more stable memory of the punishment (Cordero-Erausquin et al., 2000). However, low doses of nicotine increased latency in wild-type mice, but not in β2 knockout mice, thus suggesting β2-containing receptors are important in the effect of nicotine and help to mediate the endogenous actions of acetylcholine (Marubio and Changeux, 2000).

In another previous experiment using the Morris water maze, a learning model which evaluates spatial learning, one-year-old adult β2 knockout mice and age-matched control mice were able to locate a hidden platform equally as well; However, β2

knockout mice at 2 years of age learned at a considerably slower rate (Drago et al., 2003). There are other possible explanations of this observation aside from β2 loss causing slowed learning or dementia. In young animals, other systems might compensate for a β2-containing nicotinic acetylcholine receptor deficit; whereas, the 2 year old mice brains might lack the necessary compensatory mechanism that then result in the observed effects of a lack of β2 subunit in a spatial learning task (Marubio and Changeux, 2000).

Hippocampus

The hippocampus is part of the limbic system of the brain and is involved in consolidation of short term to long term memories (Patestas, 2006), as well as spatial learning, for example, as seen in the Morris maze experiments. (Zoli et al., 1999). It is formed from three different regions: the hippocampus prope, including zones CA1-3, the dentate gyrus, and the subiculum (Patestas, 2006). The dentate gyrus is one of two regions in the brain that undergo adult neurogenesis (Harrist et al., 2004). Additionally, studies using β2 knockout mice, showed a marked decrease in cell numbers and volume of the dentate gyrus, indicating cholingeric disruption due to the missing β2 subunit (Harrist et al., 2004). Clinically, the hippocampus is important because it is one of the most prevalent brain regions to show significant declines in cholinergic neuronal loss as Alzheimer's Disease progresses (Dani and Bertrand, 2007).

Olfactory Bulb

The olfactory bulb is located at the most rostral portion of the brain and is important in the sense of smell, or olfaction. It is composed of several layers, including the glomerular layer, the external plexiform layer the mitral layer and the granular cell

layer. Glomeruli in the glomerular layer, in concordance with mitral and tufted cells receive combinations of neuronal inputs, each coding for a distinct perceived odor (Patestas, 2006). The olfactory bulb (OB) was selected for measurements for multiple reasons. First, the OB is the second brain region to be associated with adult neurogensis. The OB is continuously supplied with new neuroblasts throughout life, however these new neurons are not produced in the OB (Mechawar et al., 2004). They migrate to the granular cell layer through the rostal migratory stream (RMS) from the subventricular zone (SVZ) located on the sides of the lateral ventricles in the forebrain (Lennington et al., 2003). If lacking the β2 subunit of the nAChRs caused an overall disruption of cell proliferation, evidence of this might be present in the OB where new neurons should be found. Decreased neurogenesis should result in decreased volume or cell density. Secondly, in-situ hybridization experiments have revealed an elevated level of high-affinity nAChRs located the OB (Drago et al., 2003) with a majority of those being of the β2 type (Mechawar et al., 2004). Therefore, it is important to survey this region for differences between β2 (-/-) and wild type mice.

MATERIALS AND METHODS

Mice

Aged and young adult male β2 (-/-) and wild type (+/+) mice were used for this study. Aged mice are defined as being 18 months of age, whereas young adult mice were 2-3 months of age. Control or wild type mice were purchased from The Jackson Laboratory, Bar Harbor, Maine. The β2 knock mice were produced at the Art Beaudet Laboratory, Baylor University, Waco, Texas, but are now commercially available through Jackson Laboratory. These mice were housed at the Texas A&M laboratory Animal Resources and Research (LARR) building. A total of 18 mice were used, 9 β2 (-/-) and 9 wild type (+/+).

Sectioning

Mice were anesthetized with isoflurane inhalant anesthesia until breathing stopped and then were decapitated. The brains were removed from the skull and rapidly frozen using powdered dry ice. Powdered dry ice was used instead of liquid nitrogen to help limit the amount of water crystallization in the cells. The frozen brains were stored at –70 °C until they were sectioned. All brains were cut into sections using a SLEE cryostat. Young adult (2-3 months old) brain sections were cut sagittally at a thickness of 18 micrometers. Aged (18 months old) brain sections were cut coronally at a thickness of 15 micrometers. Sections were thaw-mounted onto microscope slides coated with gelatin, and stored at –70 °C until staining. For the young adult mice, every 5^{th} section was used, whereas for the sections obtained from aged mice, every 10^{th} section was used.

Staining

The microscope slides with sections were warmed to room temperature and dried before staining commenced. All sections were stained using 0.1% thionin in sodium acetate buffer, which is a stain for DNA/Nissl substance. Slides were stained briefly with thionin 30-60 seconds) and rinsed with deionized water (1-3 minutes) to remove any excess stain. They were then immersed in 70% ethanol (1-3 minutes) to differentiate cytoplasm and nuclei. Nuclei retain more thionin after the ethanol wash and therefore stain darker than the cytoplasm. The slides were dried overnight, dipped in xylene and cover slipped using Permount.

Imaging

Prepared slides were coded to prevent bias in measurements between the two groups, and digitally imaged using a Nikon DXM 1200 digital camera attached to a Nikon Eclipse E400 microscope and the Nikon ACT-1 Program. A subset of measurements for olfactory bulb volumes from young adult mice were obtained using autoradiographic films exposed to sections labeled for in situ hybridization for expression of mRNA from three different genes associated with longevity: SIRT, Nampt, and Ku70.

Measurements

All sample measurements were performed using the Image J program obtained from NIH (http://rsb.info.nih.gov/ij/download.html). For brain region volume measurements, section images were captured using the 2x objective. Once opened in the Image J program, a scale was set to allow a freehanded tracing of the desired brain

region to give an area measurement in mm^2. At least two measurements were made and averaged to give a best estimate of the area. In the coronally cut aged olfactory bulb samples, only one bulb was measured to correspond with the saggitally cut young adult animal samples. These averaged areas were then used to estimate the volume of the brain region by multiplying the sum of the averaged areas of all sections for that mouse by the number of skipped sections and the thickness of the sections. For example, to find the hippocampus volume for aged mouse Z we used the following equation:

Hippocampus volume of aged mouse Z (mm^3) = **Σ** average of all sections for mouse Z (mm^2) **x** 10 skipped sections **x** 15 micrometers

For cell density measurements, ten randomly selected areas of the cell layer to be measured from each mouse were captured using the 40x objective. Then, a 100 x 100 micrometer area from the image was randomly selected. The number of cell bodies in this area was counted twice for accuracy and averaged for each animal.

Statistics

All measurements were tested for significant differences between phenotypes using an independent t-test via the Microsoft Excel 2003 Data Analysis Pack add-in. $\alpha = 0.05$. All values are averages plus or minus the standard error of the mean (SEM).

RESULTS

Hippocampus Volume of Young Adult Mice

Figure 1 shows a representative saggital of a young adult hippocampus section. Figure 2 suggests a decrease in average hippocampus volumes of young adult β2 knockout mice (8.427 ± 1.067 mm^3) with respect to wild type mice (8.911± 1.049 mm^3). However, the independent t-test showed no significant differences. P=0.605.

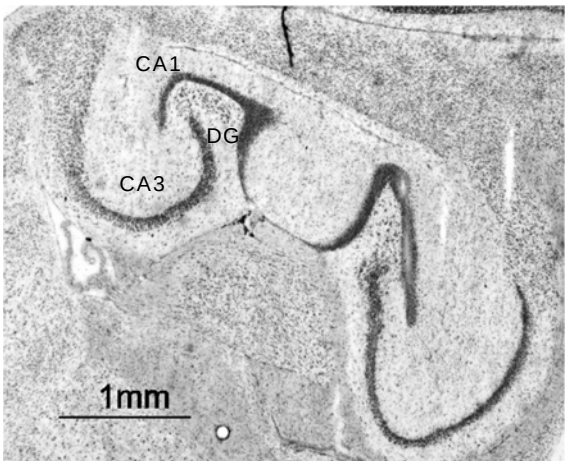

Figure 1. Nissl stained sagittal section of young adult mouse hippocampus. 2X objective. Dentate Gyrus (DG)

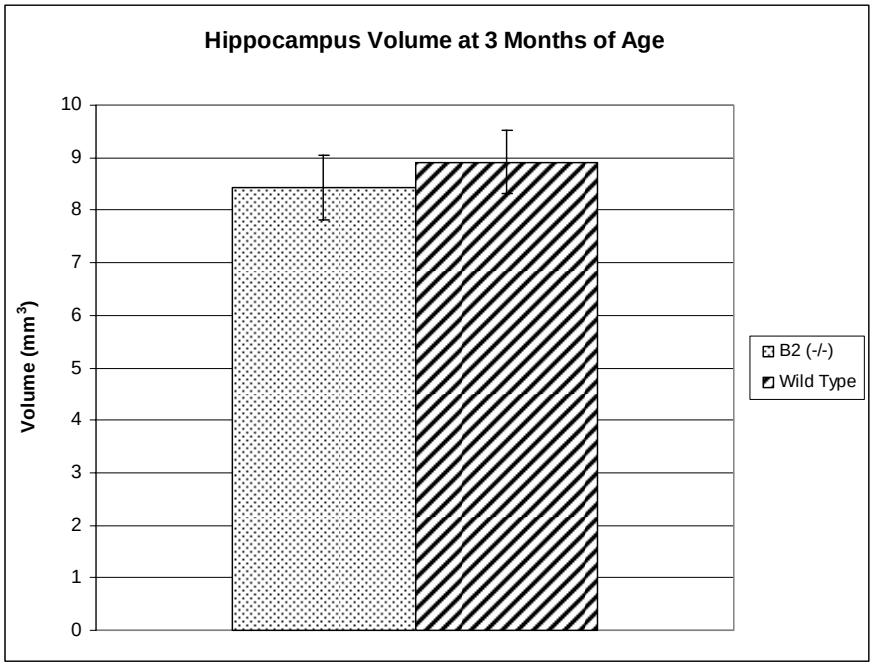

Figure 2. Hippocampus volumes at 3 months of age. Average hippocampus volume (mm^3) of young adult β2 (-/-) and wild-type mice. (n=3).

Hippocampus Volume of Aged Mice

Figure 3 shows a coronal section of an aged mouse hippocampus. It was hypothesized that aged hippocampus volumes of aged β2 knockout mice would be decreased compared to aged-matched wild type animals due to a loss of the β2 subunit's potential neuroprotective properties. Figure 4 exhibits a slight increase in average volume of the β2 (-/-) mice (12.150 ± 0.451 mm^3) compared to the wild-type counterparts (11.511± 0.878 mm^3), but this is not supported due to an insignificant t-test. The variation within the two groups is too large to give a definite tend. P= 0.532.

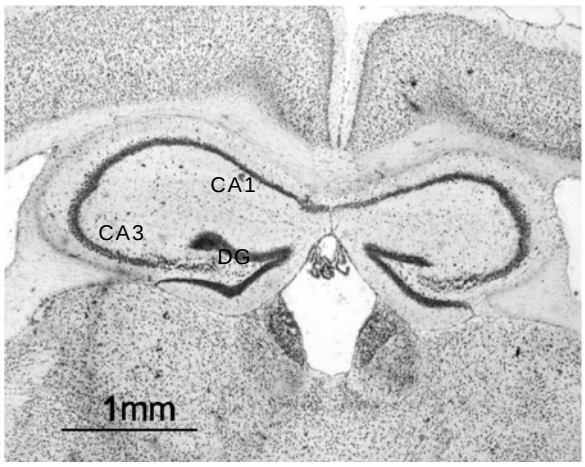

Figure 3. Nissl stained coronal section of aged mouse hippocampus. 2X objective. Dentate gyrus (DG)

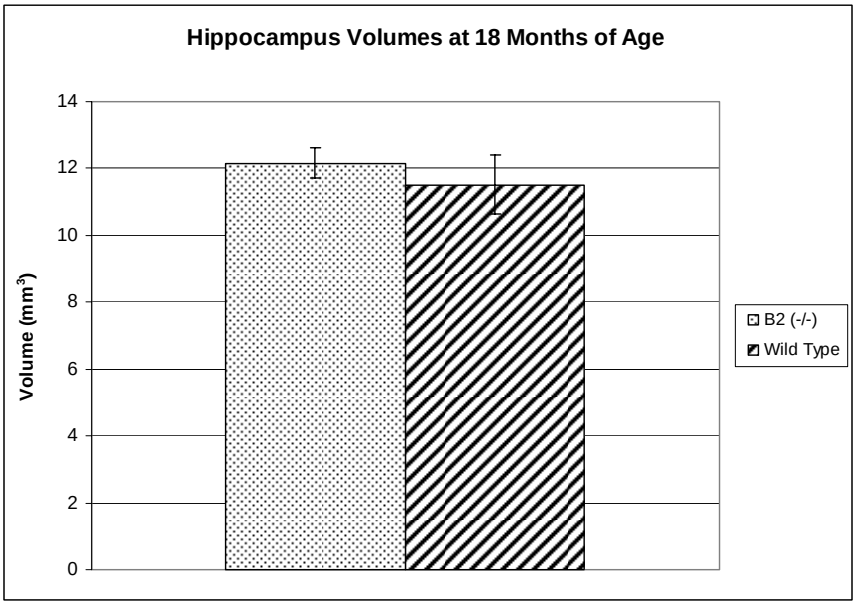

Figure 4. Hippocampus volumes at 18 months of age. Average hippocampus volume (mm^3) of aged β2 (-/-) and wild-type mice. (n=6).

Olfactory Bulb Volume of Young Adult Mice

Figure 5 shows a sagittally cut young adult mouse olfactory bulb. Figure 6 indicates an increase in OB volume in β2 (-/-) young adult mice (7.646 ± 0.859 mm^3) compared to age-matched wild-type mice (6.764 ± 1.017 mm^3); however, both groups had considerably large SEM and therefore produced a insignificant t-test. An additional subset was incorporated using previously made in situ hybridization films of the same mice sampled in this data set. An enlarged scanned image of these films could be measured according the previously outlined procedures. An example of this is seen in figure 7. P= 0.544.

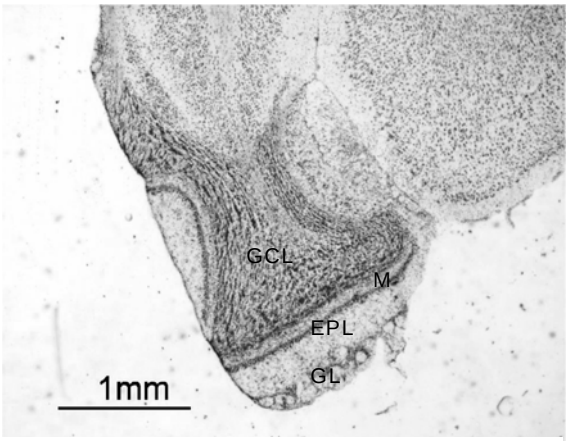

Figure 5. Nissl stained sagittal section of young adult mouse hippocampus. 2X objective. Glomerular layer (GL), External Plexiform layer (EPL), Mitral layer (M), Granular cell layer

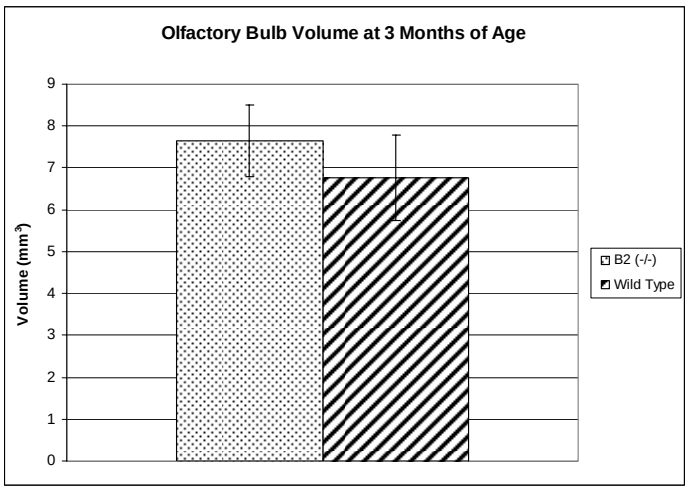

Figure 6. Olfactory bulb volumes at 3 months of age. Average olfactory bulb volume (mm^3) of young adult β2 (-/-) and wild-type mice. (n=3).

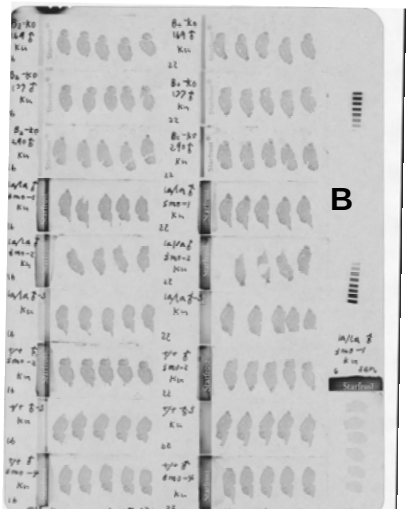

Figure 7. In situ hybridization film. (A) Enlarged sagittal section from (B) film sheet.

Olfactory Bulb Volume of Aged Mice

β2 knockout mice showed an increase in average OB volume (7.986 ± 1.009 cm^3) compared to the age-matched wild types (7.335 ± 0.230 $cm^{3)}$ (Figure 9). While the wild-type mice varied only slightly, the β2 (-/-) mice's SEM was much larger, producing an insignificant t-test. For this experiment, many sections were damaged which may have led to variation in the consistency of the measurement procedure, rendering this data set less accurate as others. An undamaged aged mouse olfactory bulb is seen in Figure 8. P= 0.574.

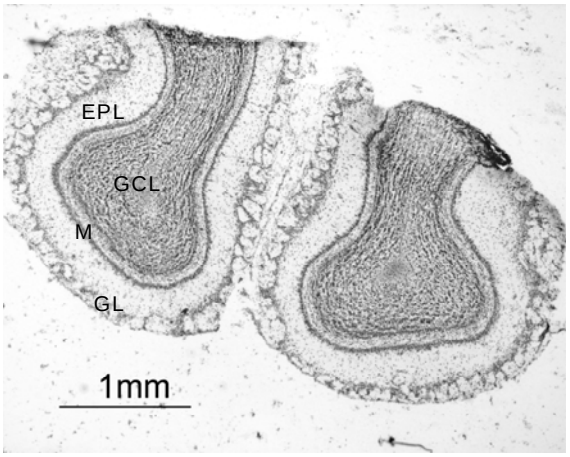

Figure 8. Nissl stained coronal section of aged mouse olfactory bulb. 2X objective. Glomerular layer (GL), External Plexiform layer (EPL), Mitral layer (M), Granular cell layer (GCL).

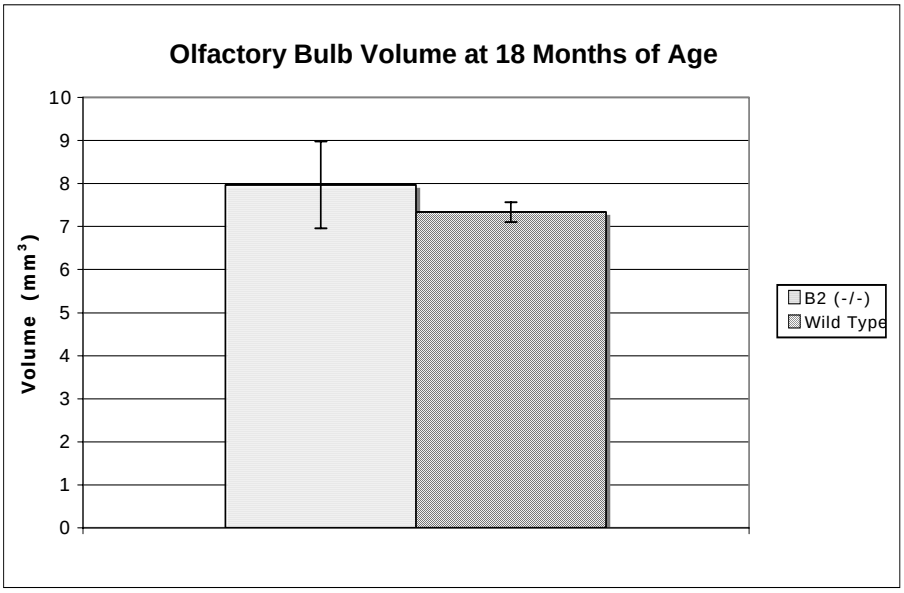

Figure 9. Olfactory bulb volumes at 18 months of age. Average olfactory bulb volume (mm^3) of aged β2 (-/-) and wild-type mice. (n=3).

Olfactory Bulb Granular Cell Layer Density of Young Adult Mice

Figure 10 shows a representative randomly selected section of the granular cell layer of a young adult mouse. Young adult β2 knockout mice showed more variation in the average granular cell density than did young adult wild-type mice, as shown by figure 11. The wild type animals exhibited, on average, a slightly denser granular cell layer (114.533 ± 2.771 cells per 10,000 μm^2) than that matched β2 (-/-) mice (111.60 ± 8.125 cells per 10,000 μm^2); however, due to β2 (-/-) variation a t-test found no significant difference between the two groups. P= 0.750.

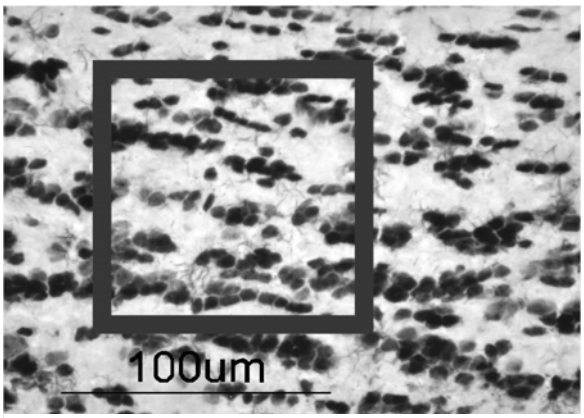

Figure 10. Nissl stained section of young adult mouse granular cell layer. 40X objective. Boxed area represents randomly selected 100 x 100 μm area.

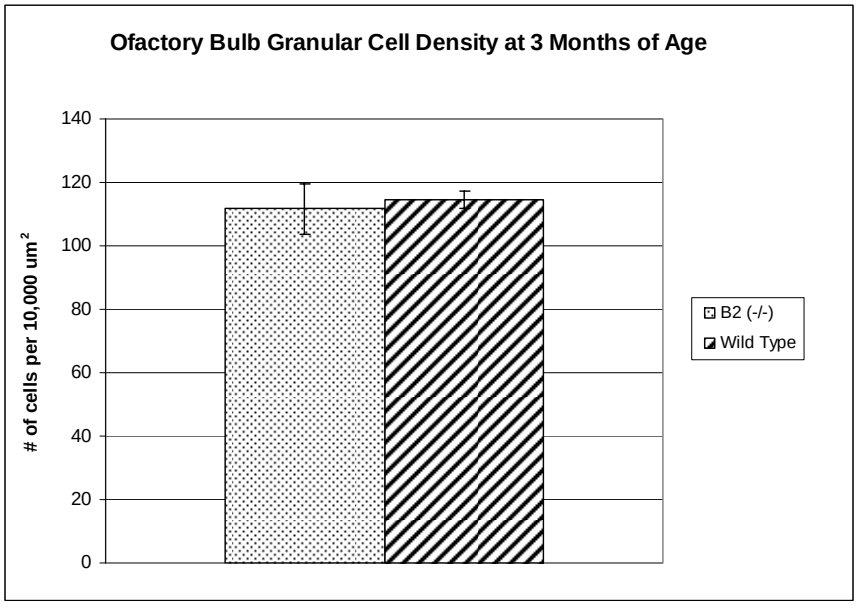

Figure 11. Olfactory bulb granular cell layer density at 3 months of age. Average count of granular cell bodies per 100 x 100 μm area per section

DISCUSSION

Summary

In summary, no statistically significant differences were found between the β2 knockout mice and the aged matched wild type mice in any of the parameters evaluated. Some of the data as presented in the figures suggest that trends towards differences between the genotypes may exist. However variations within each genotype resulted in relatively high variation and standard errors of the mean. As previously discussed, it would be beneficial to increase the numbers of animals in each experiment to help account for outlying data points and to improve the overall power of this study.

Discussion

The volumes of the hippocampus of the wild type and β2 knockout age-matched mice showed no statistically significant differences. These data indicate that the loss of the β2 subunit from nicotinic receptors located within the hippocampus does not result in excessive cell loss, which would be evident in an overall change in hippocampal volume. The decrease in hippocampus cell proliferation in adult β2 (-/-) mice reported (Harrist et al., 2004), including a decreased dentate gyrus volume, does not appear to lead to significant changes in overall hippocampus volume in either young adult, aged, wild type or β2 knockout mice. Additionally, this lack of difference is supported by von Bohlen und Halbach and Unsicker (2002). The study goes further into detail stating the CA1 and CA2/3 were insignificantly altered between genotypes and neuronal density of these areas tended to be decreased, but not to a significant extent (von Bohlen und Halbach and Unsicker, 2002). In support of this idea, recent

human epidemiological studies have shown no significant difference in hippocampus volumes between 18-85 year old healthy individuals suggesting hippocampal loss due to aging may be on a smaller scale than overall volume loss (Lupien et al., 2007).

The volumes of the OB and the OB granular cell layer density of the wild type and β2 knockout age-matched mice also showed no statistically significant differences. These findings correspond to the reported lack of difference between aged β2 knockouts and wild type OB and granular cell layer volume as presented in Mechawar et al. 2004. However, it is important to point out that aged β2 (-/-) mice granular cell layer, a parameter not measured in this study, was found to be significantly larger that their age-matched wild-type controls (Mechawar et al., 2004). As for mentioned, in situ hybridization films were used to produce more measurable sections for the young adult olfactory bulb data set. This method was discontinued because it was found that additional sections did not greatly enhance the sensitivity of the measuring methods previously used.

Finally, it was hypothesized the young adult mouse groups would show less neuronal loss than the aged mice due the proposed protective effect of the β2 subunit of the nChRs, however since no statistically significant differences were found between age groups, we cannot confirm our hypothesis.

Conclusions

Since no statistically significant differences were found in the measured areas, the hypothesis that loss of the β2 subunit of nAChRs would cause excessive cell loss and therefore reduced volumes in the regions affected by cholinergic disruptions

cannot be accepted. However, it is important to state that, at this point, it cannot be said with certainty that a lack of the β2 subunit of nAChRs does not have any effect in the CNS of β2 knockout mice, relative to wild type mice. More in-depth measurements of the β2 (-/-) mouse brain and its subcomponents must be done before any conclusions can be drawn.

Recommendations for Future Research

To further this study, granule cell density of the aged mice should be measured. Mechawar et al. (2004) found a significant increase in new granular cells in aged β2 knockout mice; however this group studied mice that were injected with BrdUrd to study cell proliferation. It would be beneficial to take a snapshot measurement of overall cell density to correlate with this study. It would also be valuable to study the cell density in different regions of the hippocampus as these regions are very diverse and have different functions pertaining to cognition.

Furthermore, this study only assessed male mice. The addition of female mice to the study may bring about interesting results in areas of the brain involved in adult neurogenesis. Recent studies have found that steroid hormones, such as testosterone and estrogen, may play a part in regulation of neurogenesis and may therefore produce different results in males versus females with respect to receptor expression (Lennington et al., 2003). The addition of more animals to each studied area would also be beneficial to increase the overall power of the study. If female mice were evaluated and found to not have any significant differences in the measured parameters compared to male mice, these mice could be added to the already accumulated information from male mice to increase the power.

In addition to volume and cell density measurement, other morphological aspects could be measured. For example, overall brain weights, brain region thickness or shape, cell and nucleus diameter could all be measured to assess morphological differences between wild type and β2 knockout mice in these brain regions. Additionally, other brain regions could be measured. These regions could include the cerebellum, occipital and frontal cortices, and the basal forebrain due to their high levels of nAChRs (Drago et al., 2003).

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EDUCATION

Texas A&M University 2004 - 2008

College Station, TX

Bachelor of Biomedical Science

Honors: Research Fellow GPR: 3.52/4.00

RESEARCH

Texas A&M Honors Undergraduate Research Fellows Program 2007-2008

Selective and highly regarded one year independent undergraduate research program

Thesis: *Survey of Neuronal Variations in Adult β2 (-/-) Knockout Mice*

- Conduct independent research project in collaboration with faulty advisor
- Use β2 (-/-) mice as model for study of neurodegeneration and aging
- Use of imagining microscope and imaging software
- Thesis to be published at Texas A&M University's repository library

LEADERSHIP EXPERIENCE

Delta Gamma Sorority Fall 2004-Present

Director of Sponsorship, *2006*

Recruitment Rotation Crew Leader, *Fall 2005*

Rituals crew, *2006-present*

Chapter purchasing crew, *2004-2005*

INTERNATIONAL EXPERIENCE

Germany History of Medicine Study Abroad Program Summer 2007

Six week program focused on German History and its impact on both human and veterinary medicine.

- Visited sites including: medical schools, veterinary schools, animal research institutes, pharmaceutical companies, museums, and historic sites.

AWARDS & HONORS

Texas A&M Association of Former Students Scholarship	Fall 2007-Spring 2008
Honors Incentive Award	Fall 2007-Spring 2008
Delta Gamma's Golden Lantern Award	Fall 2004-Spring 2006