ENHANCEMENT OF COGNITIVE DEVELOPMENT IN ND4 SWISS WEBSTER MICE BY MUSIC THERAPY

A Report of a Senior Thesis

by

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ABSTRACT

Music has been used as a stimulus to enhance cognitive functions since the time of Aristotle and Plato. Music affects both the structure and the function of the central nervous system, and current research is showing how music can be integrated within the traditional medical framework. In order to test cognitive enhancement associated with memory, ten mice were separated into two groups, a music-stimulated group and a control group. The music-stimulated group was exposed to Mozart music treatment every day from 7-11 a.m. consecutively for 28 days, whereas the control group received no music. Each group was housed in separate labs providing 12-hour light and 12-hour dark environments at a temperature of 70°F. All mice were individually run through a maze every other day, and the time to completion of the maze was recorded. As the configuration of the maze was maintained throughout the whole study, consecutive maze runs indicated the ability of each mouse to remember. A repeated-measures ANOVA found that mice exposed to music completed the maze significantly faster than those not exposed ($p < 0.0001$). For

instance, mean time to completion of the maze at day 28 was 155 seconds (+18SE) for the control group and 44 seconds (+7SE) for the music-stimulated group. These results show that music stimulus increases the rate at which the mice completed the maze, indicating that music does enhance memory.

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CHAPTER I

INTRODUCTION

Communication between the brain and the body is primarily conducted through the intricate nervous system. Impulses, in the form of action potentials, are transmitted throughout the body by billions of highly specialized neurons, or nerve cells (Butler, Lewis, & Shier, 1999). Structurally, a neuron contains a central cell body and multiple extended arms (see Figure 1). The axon, the largest extended arm of a neuron, conducts the action potential towards a muscle or adjoining neuron. If conducted to another neuron, the action potential must traverse the synaptic cleft to be received by the dendrites of the next neuron in the communication system. This constant communication system is how messages are relayed between the human brain and all the various organs and cells. The brain, the largest and most complex part of the nervous system, is the command center for all the functions of the entire body, including motor commands, mental functions, and sensations (Butler et al., 1999).

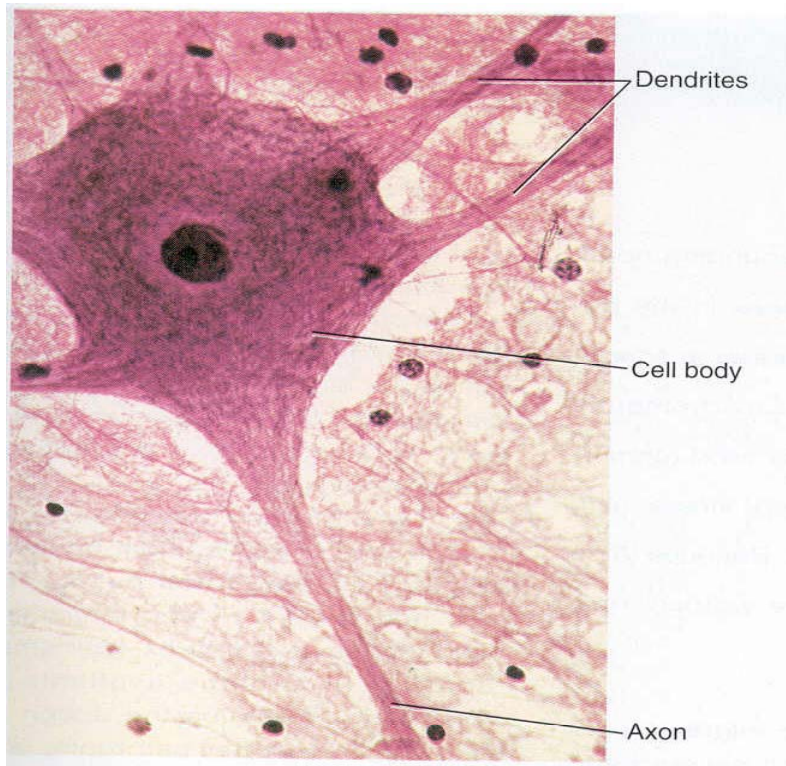

Figure 1. Structure of a Neuron (Butler et al., 1999, p. 345).

Brain Structure and Development

The correct structure and development of the brain is important in determining proper cognitive development. Lefrancois (2001) explains that sensory and cognitive stimulation and adequate nutrition determine proper brain development, which are two crucial factors in the last three months of fetal development. Sensory stimulation, such as playing music, reading or talking to the fetus, can stimulate the neuronal activity of the brain already formed in the womb. There is evidence that infants prefer the sound of their mother’s voice over others, which suggests that a fetus can hear sounds while still in the uterus and distinguish among them (DeCasper & Fifer, 1980). Infants seem to prefer higher frequencies and highly melodic expressive voices. This is apparently evident in the infant's interest and attention to parent's "baby talk," consisting of higher pitches and rising inflections (Aslin, Jusczyk, & Pisoni, 1997).

Butler et al. (1999) describe the three main structures of the brain: the brain stem, the cerebellum and the cerebrum (see Figure 2). At birth the brain stem is the most highly developed brain structure, functioning to connect more vital structures to the spinal cord. The brain stem is responsible for fundamental physiological functions such as respiratory rate and cardiac function.

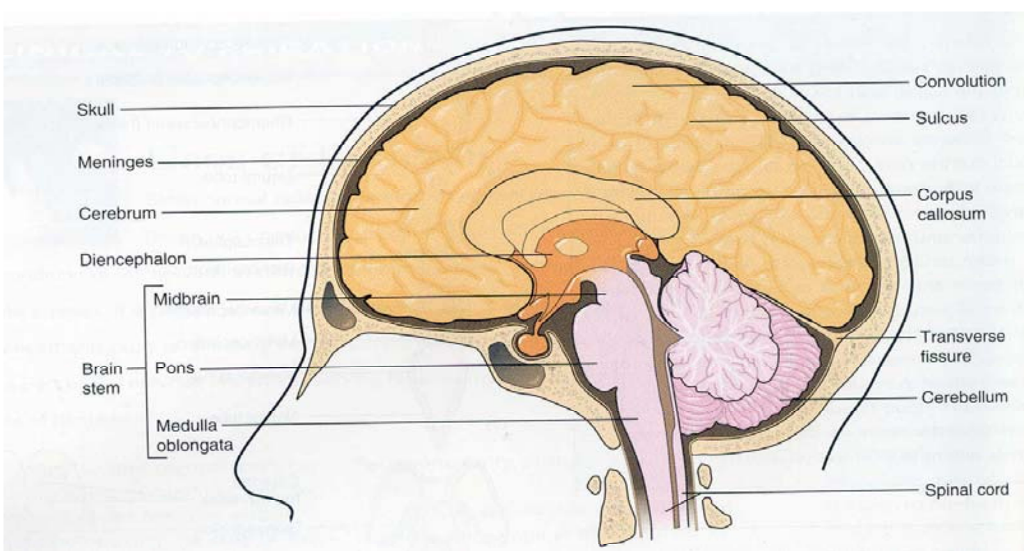

Figure 2. Structure of the Brain (Butler et al., 1999, p. 388).

The cerebellum, located at the back of the brain behind the brain stem, is responsible for balance and integration of sensory and motor functions. The cerebrum is the last to develop in the fetus, and constitutes 75% of the total mass of the brain (Lefrancois, 2001). It is responsible for some of the most important functions such as sensation, coordination, thought and language.

The cerebrum has been referred to as the structure that determines intelligence, memory and personality. The cerebrum is separated into two hemispheres, the right and left, and connected by the corpus callosum.

Fischer and Rose (1996) explain that a two-year-old child can learn an incredible amount of information within a short time period because the neurons of the entire brain region proliferate and form connections at a great rate within the first two years of life. If these neuronal connections are not made within the first two years of life, the ability to connect later on is not possible. Thus, it is imperative for toddlers to receive the stimuli they need to ensure proper or enhanced cognitive development.

Cognitive Development

Proper brain development ensures normal cognitive development. Cognitive development is the development of mental processes such as thinking, understanding, and remembering (Lefrancois, 2001). The cerebrum, the part of the brain most responsible for facilitating and executing these processes, has made evolutionary advances along with the phylogenetic change in vertebrates (Burggren, French, & Randall, 1997). For example, the cerebrum of a fish is relatively small compared to the convoluted folding of the larger cerebrum in a human (see Figure 3).

This size increase is necessary to provide adequate surface area to allow space for more neurons, which control the higher developed functions of the evolutionary advanced animals (Burggren et al., 1997). The cerebellum is also larger in more advanced animals, such as humans, allowing the intricate coordination of higher motor functions.

Motor Skills

Lefrancois (2001) examines the difference between precocial and altricial species in terms of how they develop their motor skills. Most animals are precocial, that is they are born with highly developed motor capacities. However, humans are altricial, born with relatively undeveloped motor capacities. In altricial species, development of motor skills progresses from simple reflexes to more complex, cognitively controlled ones.

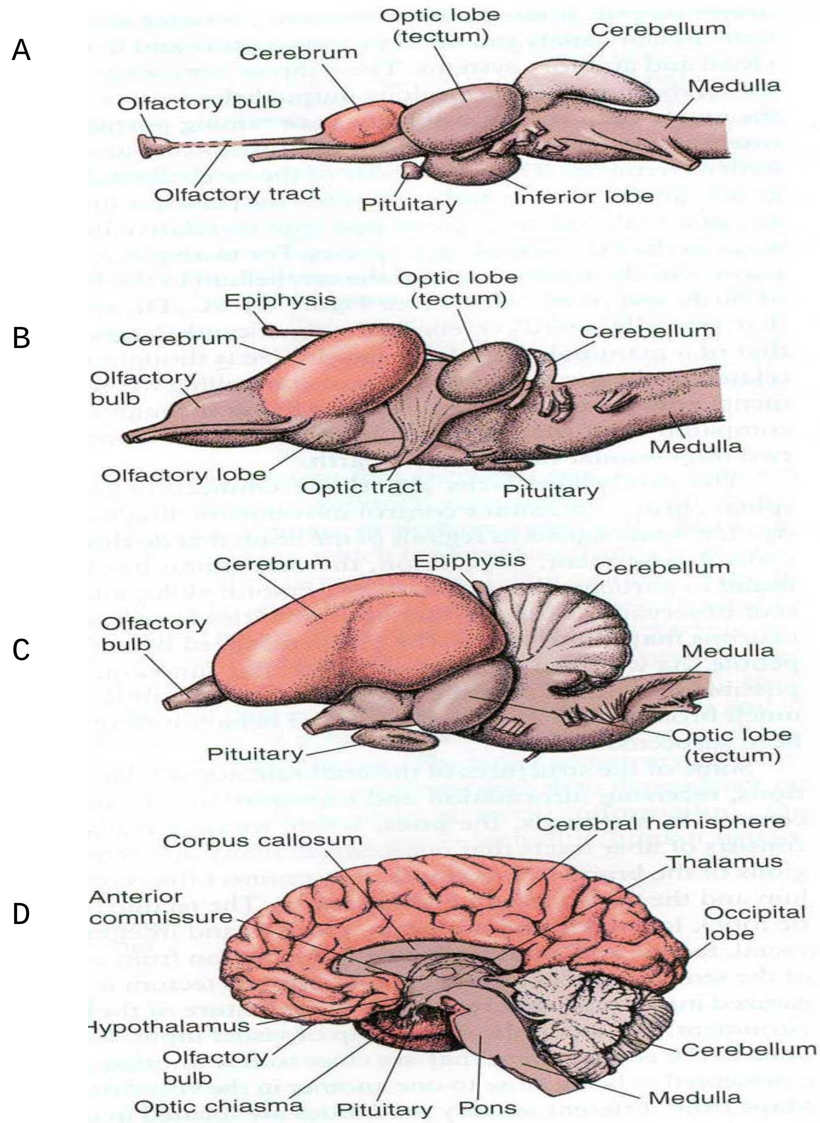

Figure 3. Cerebrum Comparisons between (A)Fish, (B)Frog, (C)Bird, and (D)Human (Burggren et al., 1997, p. 415).

Babies start out with a variety of simple reflexes. For instance, the sucking reflex is a survival reflex, which enables a baby to find food by sucking on objects put into its mouth. The Moro reflex, when a baby throws its arms and feet out and pulls them back into its body when startled, normally disappears around the baby's third or fourth month (Lefrancois, 2001). If this reflex continues to be seen when a child is older, it is a sign displaying motor impairment due to brain damage. These reflexes gradually progress into gross motor development, which involves control of muscle groups to enable an infant to crawl, walk or stand. These then develop into fine motor skills, which involve control over smaller muscle groups in order to grasp things.

Motor development reflects two major principles as described by Hughes and Robson (1996). The first is the cephalocaudal principle, which states that development proceeds from the head to the toe, explaining why babies can raise the head before controlling their fingers and toes. The second principle is the proximodistal principle, explaining the development of motor skills in an inward to outward direction, which is why children can control parts of their body closer to their center than their extremities.

Memory

The ability to remember is another important product of normal cognitive function. Memory describes the information of one's experiences that is stored for later retrieval. While learning is the acquisition of new knowledge, memory is the persistence and retention of that learning (Butler et al., 1999). Both short-term and long-term memory capabilities are created by the action of neurons and its transmission across the synapses. Therefore if the brain is damaged and the neurons cannot function properly, memory might be inhibited or disrupted.

Perlmutter (1980) describes an infant's memory as developing in three phases. The first stage is when the neurons are sending messages and habituation occurs. Habituation is when one has grown so accustomed to a stimulus that a response is no longer created. Around three months, an infant achieves recognition of objects and intended actions can be accomplished. By about eight months, the infant's memory is able to process more abstractly and symbolically. In older children and adults, memory is mostly facilitated by a sequence of organization, rehearsal and elaboration. This whole process of using one's senses to recognize an object, store it, and retrieve the same information later is not possible if there is a problem with the neural network or brain development.

Language

Language, another major component of cognitive development, is the use of arbitrary sounds that can be arranged in sequences to convey different meanings

(Lefrancois, 2001). According to Brown (1973), there are three essential characteristics of language: displacement, meaning, and productiveness. Displacement is when objects and events, actually displaced in time and space, can be represented. For example, children will be able to recall and talk about an event that happened many months ago with vivid description as if it was occurring at the present moment. Meaning is important in order to communicate because it gives a universal meaning to a particular word, so that all people within a culture can recognize and comprehend what is being portrayed. Productiveness is applying agreed-upon rules on the arrangement of words so that language is possible for everyone to understand. Language progresses from simple babbling of infants, to holophrases, then to simple sentences and finally to more complex grammatical structures of adults. If there is a neurological or brain development problem, language is often hindered or handicapped.

Organizational Disruption of Cognitive Ability

There are hundreds of diseases and disorders that cause a delay or deficit in cognitive development, as indicated by altered motor, memory, or language skills. How hindered one's cognitive development is depends on the level of destruction to the brain and the neurons that make up the nervous system. Some examples of cognitive deficit disorders include Down's syndrome, Angelman syndrome, cerebral palsy and autism.

Down's syndrome, a disorder with a triplication of the twenty-first chromosome, is the most common chromosomal birth defect occurring in about one out of every 680 live births (Lefrancois, 2001). Most Down's syndrome patients have a delay in nonverbal cognitive development, deficits in speech and language production, and auditory short-term memory (Chapman & Hesketh, 2000). These delays and deficits are due to Down's patients having an altered brain phenotype, including a smaller size of the brain and neuronal abnormalities such as diminished or reduced synapses and dendrite connections (Becker, Friend, Mito, Onodera, & Takashima, 1993).

Angelman syndrome, a disorder caused by a segment deletion of the fifteenth chromosome, can have severe cognitive and neurological impairment (Cassidy, Dykens & Williams, 2000). Many Angelman patients may never learn to speak or produce proper language development due to the underexpression or deletion of certain genes necessary to code for certain brain proteins responsible for cognitive and neurological functions (Cassidy et al.).

Cerebral palsy, especially arm-dominant hemiparetic cerebral palsy, can have major cortical and subcortical lesions causing many cognitive deficits (Humphreys, Pham, & Whiting, 2000). Memory loss and motor coordination impairments are common characteristics of this disorder.

Autistic children usually have morphological disorders of the brainstem and cerebellum, causing many linguistic and cognitive deficits (Casella, Cesari, & Muratori, 2001). Many treatment plans for autistic children are being conducted and studied.

There are many other disorders that can cause similar problems associated with cognitive development. Researchers and scientists are continuously trying to find new treatments to enhance cognitive development in developmentally handicapped persons. The medical field is incessantly trying to find a cure and proper treatment for disorders and diseases. However, mental retardation and cognitive deficit disorders are difficult to treat due to their varying levels of severity.

Enhancement of Cognitive Development

Much new research is being conducted to explore the enhancement of neural functioning and cognitive development with types of diet, medicines, and music. The United States Department of Agriculture Human Nutrition Research Center on Aging has theorized that long-term diets containing antioxidant-rich foods with phytochemicals can prevent cognitive behavioral deficits (Bickford et al., 1998). Strawberries, spinach, and vitamin E supplementation are examples of these antioxidant-rich foods (1998).

Many patients suffering from cognitive deficit disorders will receive psychiatric sessions and counseling to determine the significance of their disorder or mental retardation and the proper medicinal treatment. Pharmacologists will then try to treat a patient’s cognitive disorder with certain types of drugs. This partnership of psychiatrists and doctors working together is commonly referred to as psychiatric pharmacotherapy (Crismon, Frances, Patel, & Rush, 2001). The two departments have agreed upon the use of some psychotropic drugs, such as venlafaxine, mirtazapine, and lithium augmentation with selective serotonin-reuptake inhibitors, as a treatment for mental retardation (Crismon et al.). Many teams are formed, including surgeons, psychiatrists, physical and occupational therapists, to work together with mentally retarded patients.

Music therapy is a practice that has been used for many centuries but has just recently been organized as a profession (Diaz & Zarate, 2001). The American Music Therapy Association (1999a) defines music therapy as “the prescribed use of music by a qualified person to effect positive changes in the psychological, physical, cognitive, or social functioning of individuals with health or educational problems." Music therapists not only are trained in music theory and performance but also in psychology, anatomy, research techniques and other subjects (Diaz & Zarate). The therapeutic tool of music is primarily supportive and palliative (Lindbaek & Myskja, 2000a). However, much research is showing how music can be integrated within the traditional medical framework and actually influences central physiological variables within the body (Lindbaek & Myskja, 2000b).

History of Music Therapy

The use of music as a healing agent affecting both health and behavior has been around since the writings of Aristotle and Plato (American Music Therapy Association [AMTA], 1999b). Perhaps the first recorded instance of the effect of music therapy is found in the Book of Samuel I, when King Saul was cured of an evil spirit by David the shepherd who played music on his harp (Gaynor, 1999). In 1914, Dr. Evan O'Neill Kane, in the American Medical Association Journal, reported for the first time the use of music to calm and distract patients, as evident in the medical field by playing a phonograph during surgery (Campbell, 1997). The current music therapy program developed after World War II, when many musicians were asked to come to the Veterans hospitals to help the victims heal from physical and emotional trauma (Campbell). A curriculum was finally established and the first music therapy degree program was offered at Michigan State University in 1944 (AMTA, 1999b). The American Music Therapy Association was finally founded in 1998 (AMTA, 1999b).

Physiological Changes of Music Therapy

Music therapy has been shown to change or enhance certain physiological functions, such as breathing rate, heart rate, blood pressure and many more. Music has been shown to decrease respiratory rate, which allows one to be calm, control one's emotions, think more clearly, and have better metabolism (Lindbaek & Myskja, 2000b). Thus, music could be a beneficial tool in reducing anxiety levels (Gaynor, 1999).

Music can change the heart rate, pulse rate, and blood pressure. The human heart rate responds to music variables and thus speeds up with fast music and slows down with slower music. Blood pressure can increase as much as 10% due to excessive noise, triggering the fight or flight mechanism that releases adrenaline and norepinephrine, speeding up the heart and causing strain (Butler et al., 1999). By listening to certain musical styles, blood pressure can be reduced as much as five points (mm/Hg) and help calm the heart rate down (Gaynor, 1999).

The inner ear is connected to all the muscles in the body by the auditory nerve, which is part of the autonomic nervous system demonstrating that music being received by the ear can directly affect the body's reactions (Gaynor, 1999). Many studies have shown that music influences muscle strength, flexibility, tone, and coordination (Campbell, 1997). Music has been shown to strengthen memory and learning, stimulate digestion, affect body temperature, increase endorphin levels, boost the immune function, and regulate stress-related hormones such as cortisol and human growth hormone (Lindbaek & Myskja, 2000b).

Anatomical Influences of Music Therapy

Along with physiological changes, music also affects the very structure of the brain, which then determines cognitive ability. The brain is made up of two major hemispheres, the right and the left, which are then joined together by the corpus callosum (Butler et al., 1999). Past research has studied and theorized that the right hemisphere of the brain controls the non-speech aspect, such as hearing music with pitch and chords while the left hemisphere controls aspects such as rhythm, speech and language (Borchgrevink, 1993). However, more recent studies show that in most people both cerebral hemispheres work together to perform functions, with almost 90% of people displaying a type of hemisphere dominance (Butler et al., 1999). Usually the left hemisphere is the dominant one, controlling the language and intellectual functions (Butler et al.). The corpus callosum, connecting both hemispheres, allows both sides of the brain to receive information simultaneously.

The neural network and connections increases from birth until the age of about eleven (Lefrancois, 2001). This is one reason why it is so important for children to be exposed to language and music early in childhood. It has been shown that the corpus callosum of musicians is thicker and more fully developed, which reinforces the idea that music enlarges the neural pathways and stimulates learning (Campbell, 1997). The planum temporale, which are also more pronounced in musicians, is a part of the brain located in the temporal lobe of the cortex, responsible for processing language and categorizing sounds (Campbell). This shows more evidence to the link between language and music. Music therapy then not only affects physiological functions, but also the basic unit of cognitive ability and learning, the brain and neural network.

Examples of Music Therapy Treatments

While there are hundreds of examples and testimonies to the positive effects of music therapy, Campbell (1997) lists several places where music therapy is actively promoted and supported. In the Journal of the American Medical Association in 1995, a study was published which showed that surgeons who listened to music while operating performed mental tasks more quickly and accurately. Another great study was conducted by a professor of music and psychiatry at Kingston University in Ontario, Canada. He prescribed 15 minutes of music therapy to patients who had gone through painful operations. His results showed that these patients required only 50% of the usually recommended doses of sedatives and anesthetic drugs. A couple of places where music therapy is practiced are St. Mary's Hospital in Green Bay, Wisconsin, where they make cassette players and headphones available in all patient rooms, and at Saint Luke's Hospital in Chesterfield, Missouri, in areas of rehabilitation, intensive care, breast cancer and stroke recovery, and many other departments. With more and more research and integration within the medical field, music therapy hopes to become a standard and accepted measure of treatment.

Mozart's Music as Therapy

There are many types of music that can be used in the different treatment plans for an individual patient. One of the most widely accepted and researched music shown to produce positive effects is that of Mozart. Monks in Brittany, France, play Mozart to their animals, and the cows have produced more milk (Campbell, 1997). The Immigration Department of Washington State plays Mozart during English classes for Asian citizens, and it speeds up their learning (Campbell). Mozart was saturated with music even before he was born, a theory for why Mozart was such a powerful musician and why his music is so beneficial. His father was a music director and violinist in Salzburg, and his mother was always playing serenades for him while she was pregnant (Campbell).

Don Campbell, a classically trained musician and director of the Institute for Music, Health, and Education, has been so persuaded and convinced of the power of Mozart's music he has coined the term "the Mozart Effect" (Gaynor, 1999). "The Mozart Effect," also the title of a book written by Campbell, explains how Mozart's music increases creativity, calms tension, and helps people heal (Gaynor). Campbell (1997) relates a study done at the Center for Neurobiology of Learning and Memory in Irvine, California, in which the spatial IQ of undergraduate students increased by eight to nine points after listening to ten minutes of Mozart's "Sonata for Two Pianos in D Major." While many types of music can have positive and healthy results, Mozart seems to be a good place to start and one that has had extensive studies done already.

Music Therapy and Mice

Science is an important discipline that incorporates both research and experimentation. Many experiments performed within the field involve the use of rodents, most commonly mice. The mouse population is a relatively accessible and available specimen and holds a similar genetic make-up as human beings. Thus, the results of experiments with mice can be assessed and applied to similar conditions for humans. Music therapy, while not changing any genetic or molecular aspect of the specimen, can also be a treatment for mice and then applied to use with humans.

A high school student, David Merrell from Suffolk, Virginia, conducted a music therapy experiment on mice (Utah Festival Opera Company, 2001). Merrell was solely trying to determine the effect of different types of music on mice’s memories and motor capabilities to run through a maze. He used a treatment of classical and heavy metal music for ten hours a day for three weeks. Merrell found that the mice exposed to classical music could run the maze in a minute and a half, while the mice exposed to heavy metal took about thirty minutes and all ended up killing each other. The common laboratory mouse is an accessible and beneficial specimen to be used in scientific experiments.

Hypothesis

Based upon this research of the effects of music therapy on cognitive functions, memory and motor coordination of mice receiving this treatment should be enhanced displayed by a faster completion through a maze. There will be two groups of ND4 Swiss Webster mice: a control and an experimental that receives Mozart music every day for four hours. Based on the research that music therapy affects physiological functions and increases the neuronal activity of the brain, the treated mice should move through the maze more quickly and efficiently than those without or with less treatment. It is hoped that music therapy treatment can be further applied to those with cognitive deficit disorders, such as Down’s syndrome, by increasing their neuronal connections of the brain at an early age and stage of development. This would allow greater development in the functions of motor, memory and language skills for those that are developmentally impaired.

CHAPTER II

MATERIALS AND METHODS

Animals and Husbandry

Harlan laboratory (Indianapolis, Indiana) shipped a total of four female and six male ND4 Swiss Webster white mice of approximately three weeks of age. Upon arrival, the mice weighed between eight and twenty grams. The mice were individually kept in 25 cm x 15 cm opaque cages with steel lids and Kaytee Natural Aspen Bedding (purchased from PetSmart in Knoxville, TN) and litter was used and weekly replenished and changed. The mice were fed approximately 10 grams of Nutriphase™ mouse and rat formula (purchased from PetSmart in Knoxville, TN) every other day, and water was added as needed and changed weekly. The mice were housed in the Animal Research Facility (experimental group) and Lab 104 (control group) on Maryville College campus. These rooms were maintained at a 12-hour light: 12-hour dark environment at a temperature of 70°F. The mice were weighed once a week on a Mettler College 1300 balance.

Experimental Design

The mice were divided into two groups: the control group and the experimental group receiving music stimuli. In order to make the two groups as unbiased as possible, they were randomly separated with each group consisting of three males and two females. Before the music stimulus or treatment began, all the mice were run through a standard maze to determine memory proficiency at that time (see Figure 4). The experimental group received four consistent hours of Mozart music (see Appendix A) daily from 7-11 a.m. Every second day all mice were run through the maze with a reward of peanut butter

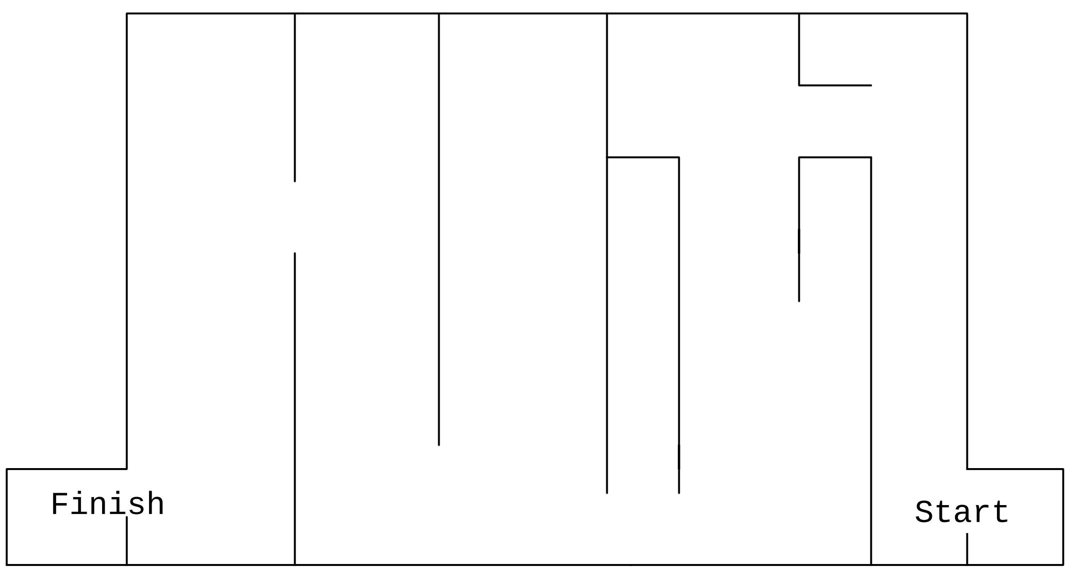

Figure 4. Maze Configuration Throughout the Study

available at the end of the maze. Times were recorded for how long it took each mouse to complete the maze run. The configuration of the maze was maintained throughout the study, allowing one to determine the efficacy of memory and/or learning for each individual mouse. The experiment was conducted for 28 days.

Statistical Analysis

Standard statistical tests were used to determine the significance of the data. A _t_-test (Microsoft Excel) was used to compare the males and females' time of maze completion at day zero. A repeated measures-analysis of variance (Statview Statistical Software) was used to compare time of maze completion between the music-stimulated and control group due to both the music stimulus and weight gain. The data was compiled, analyzed and then displayed in tables and figures.

CHAPTER III

RESULTS

Once all the data were collected, several statistical analyses were performed. Three response variables were compared and analyzed: (1) time of maze completion between males and females, (2) weight change in the music-stimulated versus control group, and (3) time of maze completion between music-stimulated and control group.

Males and females showed no significant difference in time to maze completion at day zero ($p = 0.7242$, see Table 1 and Figure 5). Weight gain was not significantly different between the music-stimulated group and the control group ($p = 0.5563$, see Table 1 and Figure 6). Time of maze completion, however, was significantly different ($p < 0.0001$) between music-stimulated and control groups (see Table 1 and Figure 7). As seen in Figure 7, after day five, the music-stimulated group completed the maze runs faster than the control group. From this point until the end of the experiment, the music-stimulated group consistently continued increasing its time, while the control group varied its time with every run. Additionally, the variances also seen in Figure 7 between the two groups showed a significant difference. At the end of the experiment, the music-stimulated group had a very small variance of +7SE, while the control group had a variance of +18SE. Thus, all the mice in the music-stimulated group were consistent with each other, while the control group mice had a wide range of times for the maze completion.

Table 1.

The Significance of the Three Response Variables Measured and Analyzed During 28 Days of Testing.

Test Analyzed	Degrees of Freedom	P-Value
Gender Differences	13	0.7242
Weight Effect	6	0.5563
Music Effect	26	< 0.001

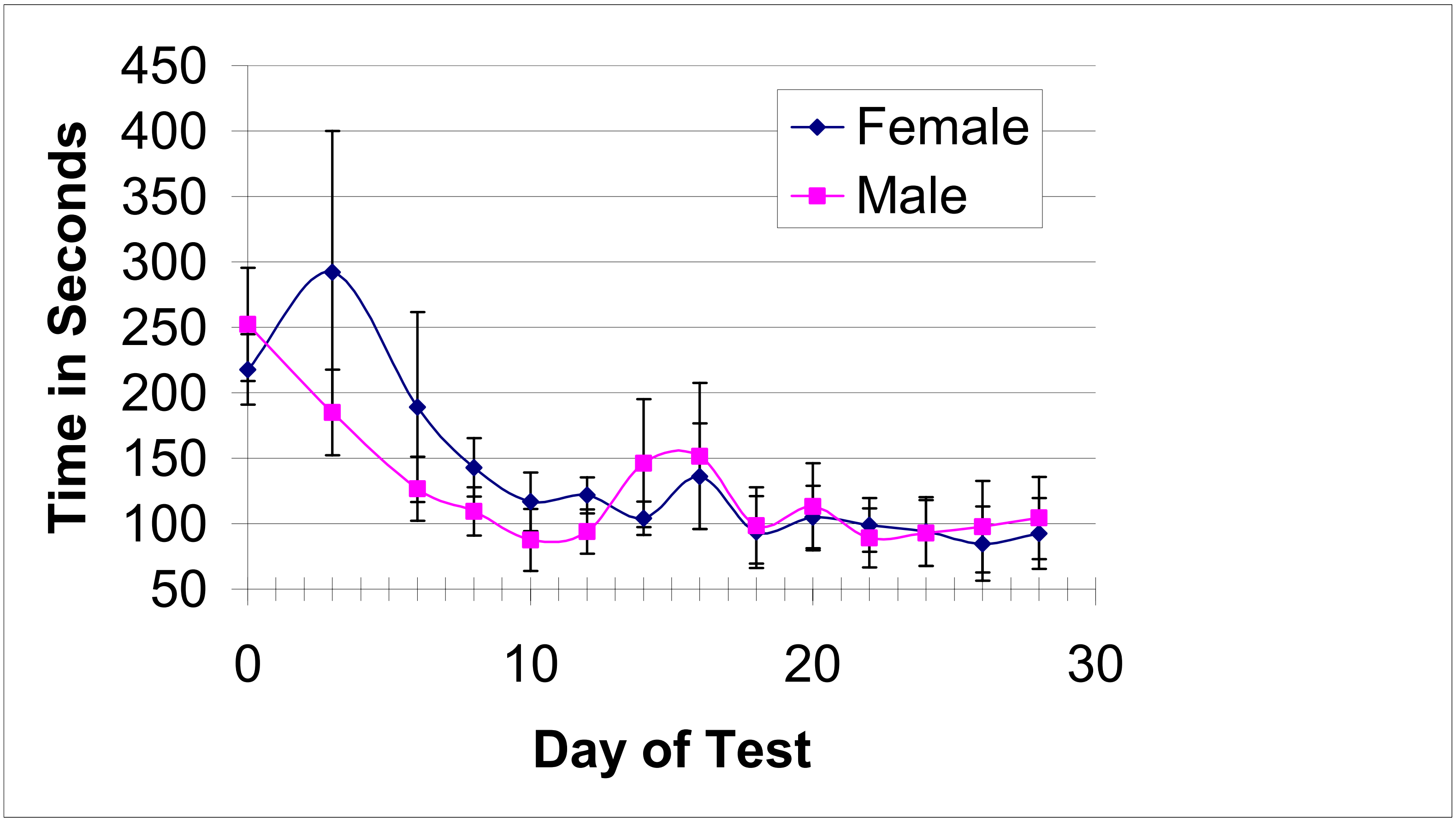

Figure 5. Average Times (+1SE) for Completion of Maze Between the Males and Females.

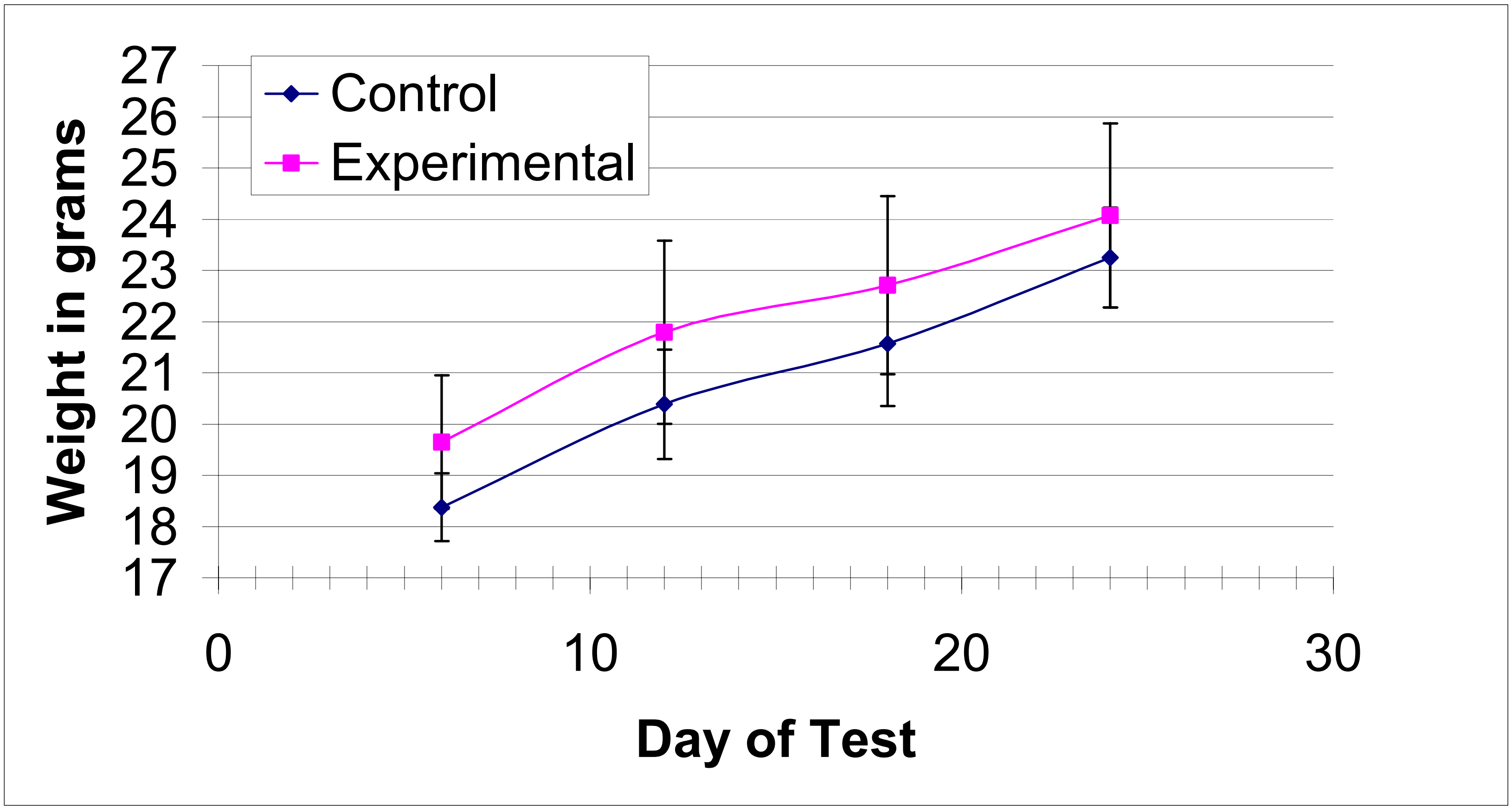

Figure 6. Average Weight (±1SE) Measured Over Four Weeks

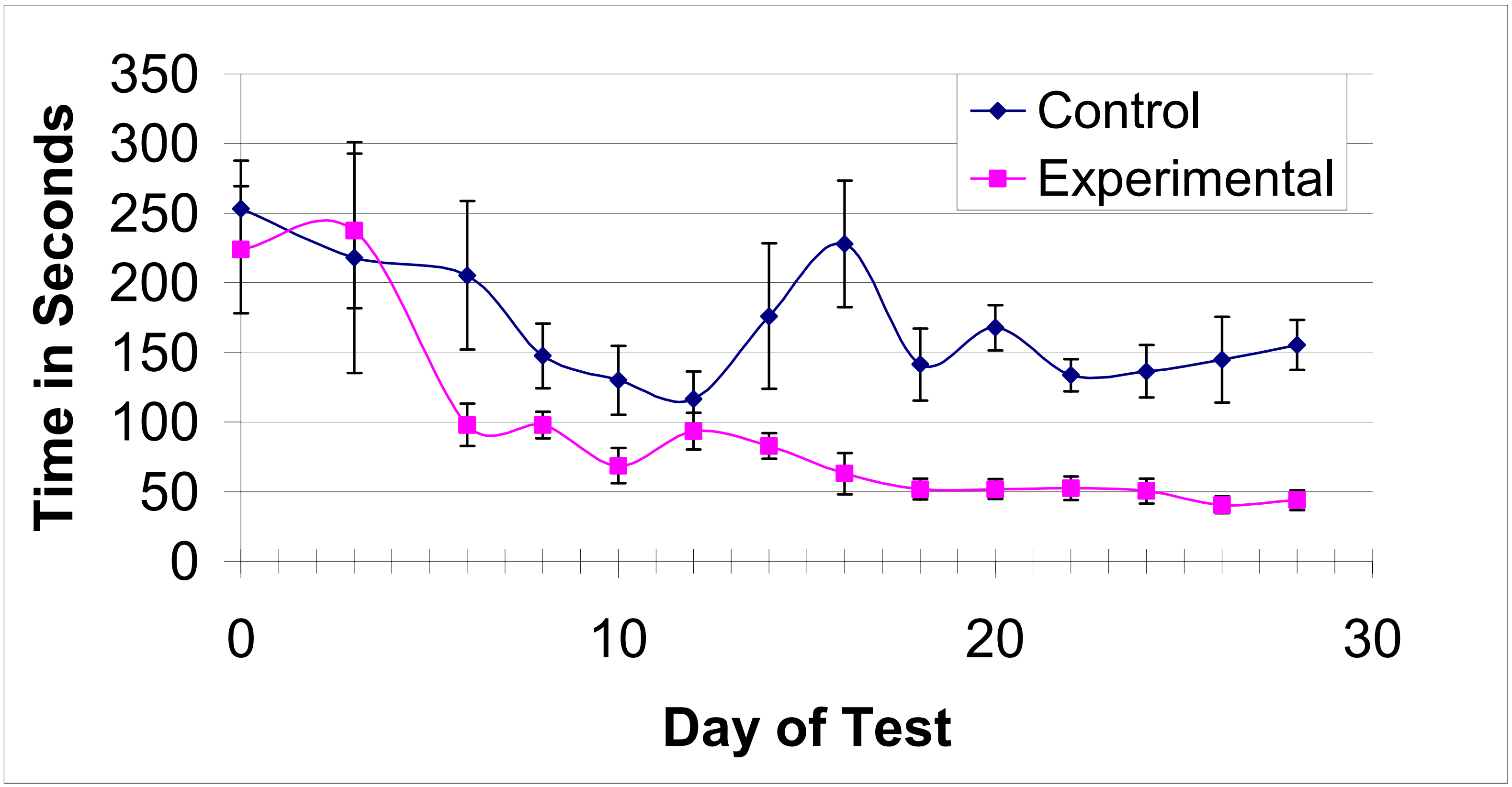

Figure 7. Average Times for Completion of Maze (+1SE) Between the Control and Experimental Groups.

CHAPTER IV

DISCUSSION

In order to determine that there were no other factors affecting the results of the music stimulus, both gender and weight effects were considered in the analysis. At day zero of the experiment, there was no difference in time to completion of the maze between males and females ($p = 0.7242$). Thus, gender was not considered as a factor for the experiment. A similar experiment on the effects of music stimuli using ninety mice also showed no gender effects for any time of maze completion (Jens, Rauscher, & Robinson, 1998). In the present study, males and females maintained comparable times throughout the entire experiment, also supporting the fact that even when the music stimulus was added it did not have a greater effect on one particular gender.

Weight gain was analyzed to determine if music stimulus influences it. There was no significant difference between the music-stimulated group and the control group in terms of weight throughout the experiment ($p = 0.5563$). Jens et al.(1998) also found no weight change differences between groups. They had originally hypothesized that the non-Mozart groups were stressed and would gain weight due to not being part of the enriching environment of Mozart music. However, the fact that there were no body weight differences among all the groups reduced the likelihood that stress was a factor (Antelman & Rowland, 1976). In the present study, due to the fact that all mice were fed the same amount of food during the three weeks, all mice in both groups experienced comparable weight gain.

The significant difference that was observed ($p = <0.0001$) was for the time of maze completion between the music-stimulated group and the control group. At day three, there was not a major difference. However, by day six, after five days of the music stimulus, there was already a significant difference between the two groups, with the music-stimulated mice completing the maze in an average of 100 seconds and the control group in an average of 210 seconds. The music-stimulated group continued to increase their time and increase the difference in time from the control group. By day 28, the last test day, the music-stimulated mice were averaging completion of the maze in less than 50 seconds, while the control mice were still averaging above 150 seconds. It was expected that over time, all mice would decrease their time due to repetition and learning processes, and this was seen in the experiment. Similarly, Jens et al.(1998) found that rats exposed to Mozart music reached the goal box more rapidly and with fewer errors than the other rats exposed to different types of music.

The question remains then, why does music have such a profound effect on learning processes and memory enhancement and what exactly are the mechanisms by which this happens. It has been accepted for a long time that environmental enrichments have positive effects on human cognitive abilities (Devaney, Ellwood, & Love, 1997). This is one reason why it is stressed to expose children to music early in their development (Lefrancois, 2001). Research and tools, such as EEG technology and brain imagining techniques, have been able to show the affects of music on the development of cortical areas (Jens et al., 1998). For instance, the corpus callosum is thicker and more fully developed in musicians than non-musicians showing that music affects the neural pathways (Campbell, 1997). Musical activity actually strengthens inherent neural firing patterns (Jens et al.). Bird and Schreckenberg (1987) found abnormal neuronal overdevelopment in the hippocampus of mice exposed to rhythmically, non-synchronized music. These mice performed worse in the maze completion than mice exposed to rhythmically, synchronized music such as Mozart. Still, little is known about the neural mechanism underlying the effect of music on the brain and creating the apparent and evident neural plasticity that takes place (Jens et al.). However, based upon the results in the present study, it is evident that the Mozart music enhanced the cognitive ability of the mice to remember the maze from previous runs and thus complete it faster every run they made. The control group that did not receive any music stimulus and thus no cognitive enhancement took almost four times as long to complete the same maze run. So while the actual mechanisms might not be clearly defined, there are obvious definite changes that music makes in cognitive functions affecting memory.

Another example of the enhancing effects of music is the observed larger left planum temporale in musically trained subjects than in untrained subjects (Huang, Jancke, Schlaug, & Steinmetz, 1994). The planum temporale is the part of the brain located in the temporal lobe of the cortex responsible for processing language and categorizing sounds (Campbell, 1997). Also, the cortical representation of the fingers of the left hand is larger for string players than for controls (Elbert, Pantev, Rockstroh, Taub, & Wienbruch, 1995). Thus, these observed effects and anatomical changes show a direct connection between music and biology. However, there is not much research focusing on the neurobehavioral effects of auditory enrichment, especially music (Jens et al., 1998).

Even though there is evidence supporting the idea that music causes physiological and anatomical changes in the brain, Mozart has been the primary type used in studies. Mozart himself was inundated with music stimuli in utero, one possible explanation as to why he was such a talented musician and why his music is very intricate and beneficial for use as therapy (Campbell, 1997). Mozart’s music includes major intervals and chords, along with complex scales and melodies providing increased creativity, a calming effect and therapeutic sounds (Gaynor, 1999). In prior studies with humans, Mozart music produced short-term enhancement of spatial-temporal reasoning when compared to repetitive works and silence (Ky, Rauscher, & Shaw, 1995). Campbell (1997) relates a study done at the Center for Neurobiology of Learning and Memory in Irvine, California, in which the spatial IQ of undergraduate students increased by eight to nine points after listening to ten minutes of Mozart’s “Sonata for Two Pianos in D Major,” coincidentally the same piece used for the experiment conducted by Jens et al. (1998). While Jens et al. tested mice listening to complex music (Mozart), minimalist music (a Philip Glass composition), and white noise or silence, the group with the fastest maze completion results were only the mice exposed to Mozart. As seen in the present experiment, Mozart music definitely had a positive effect on the mice exposed to it as seen in the increased time of maze completion.

This study showed a significant difference in time of maze completion between the Mozart-stimulated mice and the control mice, thus signifying increased or enhanced cognitive abilities for long-term memory and spatial tasks. While Mozart music was used for this study, future research should apply other types of music and observe the effects. As more and more studies and experiments are performed, greater understanding of the anatomical effects of music on the brain will be determined. This could have very strong implications for education and enrichment programs, especially where children and those with cognitive deficits are concerned. The impacts of music on cognitive development and functioning are only beginning to be unveiled.

APPENDICES

APPENDIX A

Music therapy: Mozart

Song Title (Length)

1. Flute Concerto No.1 in G (8:28)
2. Piano Concerto No.23 in A (7:01)
3. Horn Concerto No.4 in E-flat (4:11)
4. Symphony No.31 in D (6:14)
5. Piano Concerto No.15 in B-flat (4:55)
6. Violin Concerto No.4 in D (6:53)
7. Wind Serenade No.12 in C minor (4:21)
8. Concerto for Flute and Harp in C (8:23)
9. Piano Concerto No.27 in B-flat (6:57)
10. Symphony No.34 in C (8:43)
11. Fantasia in D minor (7:17)

Songs were repeated in this order for four hours.

APPENDIX B

MARYVILLE COLLEGE
HUMAN AND ANIMAL SUBJECTS REVIEW COMMITTEE
ANIMAL STUDY APPLICATION FORM

1. Student Name: Erin Verhofstadt

2. Date: October 28, 2001

3. Senior Thesis Advisor: Dr. Crain

4. Pain or Distress Category: B. (See listing of Pain or Distress Categories below)

For categories C,D, or E, USDA regulations require that the investigator consider alternative procedures. Please provide a narrative (for instance the end of Chapter 1) describing the methods and sources used to determine that alternatives are not available. If a computer assisted literature search was conducted, provide the names of the database(s) and date(s) of the search.

PAIN OR DISTRESS CATEGORIES

A. ACUTE STUDIES
Studies performed under anesthesia from which the animals are not permitted to regain consciousness, or performed on excised animal tissues collected under anesthesia or following euthanasia.

B. PAIN OR DISTRESS - NONE OR MINOR
Chronic studies that DO NOT involve survival surgery, induction of painful or stressful disease conditions, or pain or distress in excess of that associated with routine injections or blood collection. Included are induction or transplantation of tumors in animals (so long as the tumors do not cause pain and the animals are terminated prior to becoming seriously ill), administration of mildly toxic substances or drugs that cause no significant disease or distress, and antibody production as long as significant disease does not result and antigen booster doses do not include Complete Freund's Adjuvant (CFA).

C. PAINFUL PROCEDURES WITH ANESTHESIA/ANALGESIA
a. Survival surgical procedures.
b. Painful or potentially painful non-surgical procedures; e.g. bone marrow taps, injections into particularly sensitive areas such as foot pads, cardiac punctures, or traumatic procedures such as burns (burns may be category D, depending on severity).

D. MODERATE DISTRESS OR PAIN GENERALLY WITHOUT ANESTHESIA/ ANALGESIA/ TRANQUILIZERS
Induction of moderately distressful or painful disease conditions (examples: arthritis, administration of toxic chemicals, infectious challenges, immunosuppression resulting in infectious disease, peritonitis, severe inflammation, especially of weight bearing surfaces or resulting in external sores), whole body irradiation, stress models, septic shock, hypotensive shock, moderate painful stimuli (examples: low level electrical shock or heat), survival surgical procedures that have the potential to result in long term distressful illness (organ transplants, for example), induction of cardiac ischemia, booster immunizations with CFA, tumor induction or animal cultures that cause significant distress or pain, sight deprivation, restraint for periods longer than 12 hours.

E. INTENSE SUSTAINED OR REPEATED PAIN WITHOUT ANESTHESIA/ANALGESIA
Direct stimulation of CNS pain tracts, nociceptor stimulation by physical or chemical means that causes severe pain (e.g., corneal abrasions), or any category C (see above) procedure if performed without chemical relief of pain.

5. Species to be used: ND4 Swiss Webster Mice

6. Age of animals: Weight: 21-24 grams

7. Number of animals in study : 20 mice

8. Duration of study: Three months, January-March 2002

9. Location of animals during the study (building and room) Sutton Science Center, Room 130

10. List personnel to call if problems with animals develop:

Name	Daytime Phone	Nighttime Phone	Emergency No.
Dr. Drew Crain	865-981-8238	379-1706	
Erin Verhofstadt	865-981-8678	981-8678	

Investigator Assurance

The information provided in this protocol form accurately reflects the intended use of animals for this research activity. Significant changes in procedures will not be undertaken without prior notification and approval of the Human and Animal Subjects Review Committee.

All persons involved in the use of animals on this protocol have been informed of the experimental objectives and methods. Each has received training in the execution of animal-related procedures he/she will perform prior to participation in the protocol, and will participate in any educational or training programs deemed appropriate or necessary by the Human and Animal Subjects Review Committee.

I agree to follow the provisions of the Animal Welfare Act and the guidelines of the National Institutes of Health on the care and use of laboratory animals.

I agree to use anesthesia, analgesia and tranquilization to relieve pain or distress whenever use of these agents will not jeopardize the scientific validity of the data. I have specifically consulted with the Human and Animal Subjects Review Committee regarding any experiments that are classified in pain/distress categories C, D, or E.

I will take appropriate steps to avoid exposure of persons working with these animals to any biohazardous agents used in the study.

State the reasons if you cannot attest to the accuracy of any of these statements:

11. HUSBANDRY REQUIREMENTS: Is anything other than routine care and equipment required?
YES_X_ No ___ If "YES", please list below.

Music and a music player.
A maze for the mice.

12. Is it likely that pain/discomfort will be experienced by animals in this protocol?
YES___ NO_X_If "YES", describe:

13. What will happen to the animals at the end of the study? If euthanasia is required, state the methods.
I will find them all homes.

14. Briefly describe your proposed research project (or attach a research proposal). Be sure to include a justification for the species and number.

I will be testing to see whether or not music therapy can increase the rate and accuracy of cognitive development and motor functions. I will have 20 mice, ten of which I will treat with music therapy and ten which I will not. I will test the affects of the music therapy by running both sets of mice through a maze and comparing the time and completion it takes them. ND4 Swiss Webster mice are being used because they are the most common laboratory mice used for testings. My results of this study will determine whether or not music therapy is a beneficial treatment and its effectiveness for cognitive deficit disorders and diseases.

This project has been reviewed by the Maryville College Human and Animal Use Committee.

Nov 28, 2001

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