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Physical activity as a behavioral treatment in SHR rats: An animal model of ADHD

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PHYSICAL ACTIVITY AS A BEHAVIORAL TREATMENT IN SHR RATS: AN ANIMAL MODEL OF ADHD

A Thesis

by

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ABSTRACT

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Attention Deficit Hyperactivity Disorder (ADHD) is a commonly diagnosed psychiatric disorder defined by inattentive, hyperactive, and/or impulsive behaviors, typically treated with medications. Physical activity has been investigated as a treatment for children with ADHD and provides the ability for the individual to use it as a lifetime treatment option. Animal models can control for many of the issues posed by using human subjects. This study investigates whether physical activity in the form of wheel running reduces hyperactivity in an animal model of ADHD, the Spontaneously Hypertensive Rats (SHR), compared to its control, Wistar Kyoto rat (WKY). Using an ABAB design, hyperactivity was measured using an open field test and physical activity was measured by a running wheel. Results indicated wheel running had little effect on hyperactivity, however, findings proposed that hyperactivity increased with age in SHR rats. Results are discussed, limitations are recognized, and future research is suggested.

DEDICATION

This degree could not have been accomplished without the love and support of my family and friends. First and foremost, to God, my faith has never been stronger and this degree is yet another milestone in his plan for my life. To my wonderful mom, who taught me that one of the most important things in life is an education, and who supported me throughout my educational journey and always pushed me to do the best I can. Also, to my friends, thank you for being so understanding during my study days. And to my fiancé Matthew, thank you amor for being there for me, lending an ear and encouraging me during the times I thought school got tough, and for being patient and understanding throughout my college career. I love you all. And finally, to present and future behavior analysts, let's make a difference.

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TABLE OF CONTENTS

LIST OF FIGURES

Page

CHAPTER I

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD)

Attention Deficit Hyperactivity Disorder (ADHD) as defined by the most recent version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (American Psychiatric Association, 2013), is a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by inattention, and/or hyperactivity and impulsivity. The DSM-V (APA, 2013) defines Inattention as six or more of the following symptoms: A. Failing to give close attention to details or making careless mistakes in schoolwork, occupational assignments, or during other activities; B. difficulty sustaining attention in tasks or play activities; C. does not seem to listen when spoken to directly; D. does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace; E. difficulty organizing tasks and activities; F. avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort; G. loses things necessary for tasks or activities; H. easily distracted by extraneous stimuli; I. forgetful in daily activities.

For hyperactivity and impulsivity, the DSM-V (APA, 2013) includes the same requirement for the definition of inattention in six or more of the symptoms it lists. There's an extra notation that states the symptoms "must not solely be a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions." For older adolescents and adults, at

least five symptoms are required. The symptoms for hyperactivity and impulsivity include: A. often fidgets with or taps hands or feet or squirms in seat; B. often leaves seat in situations when remaining seated is expected; C. often runs about or climbs in situations where it is inappropriate; D. often unable to play or engage in leisure activities quietly; E. is often "on the go" acting as if "driven by a motor"; F. often talks excessively; G. often blurts out an answer before a question has been completed; H. often has difficulty waiting a turn; I. often interrupts or intrudes on others. The DSM-V (APA, 2013) requires symptoms be present before age 12, present in two or more settings, and do not occur exclusively during the course of schizophrenia or are not better explained by any other disorder. These symptoms must have persisted for at least 6 months to a degree that is inconsistent with the individuals developmental level. In addition, the symptoms have a negative impact on social and academic/occupational activities.

In regards to specificity of the disorder, the DSM-V identifies three subtypes. If symptoms are mostly inattentiveness, then the individual receives a diagnosis of predominantly inattentive type (ADHD-PI). If symptoms are mostly hyperactive/impulsive, then the individual receives a diagnosis of predominantly hyperactive/impulsive type (ADHD-HI). If the individual displays a combination of both criteria, then they receive a diagnosis of combined type (ADHD-C) (APA, 2013).

ADHD is an important disorder to research because the rates of this disorder have increased significantly over time. Rosemond and Ravenel (2008) reported that in the past 25 years, rates of diagnosis had gone from 1 in 33 children to as high as 1 in 10. Children with this disorder also run the risk of being diagnosed with comorbid disorders such as anxiety (Amiri et al., 2013, Yoshimasu et al., 2012), conduct/oppositional defiant disorder (Amiri et al., 2013,

Yoshimasu et al., 2012), mood disorders (Yoshimasu, 2012), and/or sleep disorders (Golan et al. 2003; Silvestri et al., 2009). These comorbid disorders may also require medication to treat them effectively, while some of these disorders may be a side effect of the medication (Kraut et al. 2013, Takeda et al. 2012, Yoshimasu et al. 2012). In a study conducted by Yoshimasu and colleagues (2012), they found that 60% of their sample population had at least one comorbid psychiatric condition and 35% had two or more. This study also reports gender differences in comorbidity, with internalizing disorders, such as anxiety disorders, being more apparent in girls, and externalizing behaviors, such as Oppositional Defiant Disorder (ODD)/Conduct Disorder (CD), being more apparent in boys. The study also indicates that there is a coexistence of externalizing and internalizing disorders. Comorbid disorders along with ADHD have been found to increase with age, and ODD has been found to occur in all ages (Takeda et al., 2012). In a study by Amiri and colleagues (2013), 62.5% of their population had psychiatric comorbidity. In this study they found chronic motor tic disorder, ODD, and specific phobia were related to all subtypes of ADHD. They also pointed out age variability in prevalence of comorbidity. If early intervention is applied to individuals with ADHD, it is believed that comorbidity can be reduced.

Treatments with Individuals

As the rates of diagnosis rise, so do the rates of distribution of prescription stimulants, and the most commonly prescribed treatment for ADHD is stimulant medication (Kraut, 2013; Weiss et al., 2010; Winstanley et al., 2006). These medications include methylphenidate (Ritalin), d-methylphenidate (Focalin), d-amphetamine (Dexidrine), and mixed amphetamine salts (Adderall) (Ryan et al., 2011; Vaughan et al., 2009). Stimulant medication has the greatest effect size for treating core symptoms of ADHD (MTA Co-Op group, 1999). Medications are

most likely used because they are fast acting. The onset effect is usually within 30-45 minutes of administration (Vaughan et al., 2009). Also, the duration of the effects of these medications typically last anywhere between 4 to 8 hours, depending on the release rate (Ryan et al., 2011). Singh and colleagues (2010) conducted a study in which they conducted focus groups to explore the experiences and perceptions of young people on stimulant medication. In adolescents and young adults, there is a sense of awareness of these symptoms, and they know why some of these behaviors are problematic to a certain degree. In this population, medication is perceived as a less stressful way of managing the behaviors associated with this disorder (Singh et al., 2010). Medications are also commonly used because stimulants tend to produce reductions in ADHD behaviors (Spencer et al., 2005). Since ADHD is most commonly first identified by parents and teachers (DSM-V, APA, 2013), they are the primary source of identifiable information concerning the subjects in these studies. In a study conducted by Ryan and colleagues (2011), researchers reported that both parents and teachers noticed improvements in their student/child's symptoms while they were taking medication.

Although medications seem to be an effective way of treating ADHD symptoms, there are some important side effects that should be mentioned. For example, research regarding the effect of stimulant use for this disorder includes addiction and misuse (Cortese et al., 2013; Lakhan et al., 2012; McCabe et al., 2006), stunted growth in children (Cortese et al., 2013; Ptacek et al., 2009), and cardiovascular issues (Elia et al., 2010). Evidence of long-term effects of use is near to non-existent. In addition, the stimulants produce side effects such as loss of appetite (Peterson et al., 2008; Vaughan et al., 2009), irritability (Firestone et al. 1998), trouble sleeping (Vaughan et al., 2009), and possible serious neurological issues (Wang et al., 2013).

Given all of these side effects, frequently additional prescription medications are used to reduce these issues (Amiri et al., 2013; Takeda et al., 2012). Another issue that arises along the lines of medication is that children with ADHD grow up to be adults with ADHD, making it difficult to ensure accurate dosage over time as their bodies tend to build a tolerance to the medications that are used (Ross et al., 2002). Some studies have found that high doses of stimulant medication could result in psychosis (Cortese et al., 2013), seizures (Cortese et al., 2013), cardiovascular events (Cortese et al., 2013; Elia et al., 2010; Raga et al., 2013), and induction of schizophrenic-like states (Lakhan et al., 2012). As stated previously, medication is not the only option for treatment, only the most prevalent.

Also available as a pharmacotherapeutic treatment is the use of non-stimulant medications. These include Tricyclic antidepressants (TCAs), non-tricyclic antidepressants, specific norepinephrine reuptake inhibitors, alpha-2 noradrenergic agonists, non-schedule stimulants, and others (Budur et al., 2005). These pharmaceutical options are used for individuals who are unresponsive to stimulants, are against stimulant use, have comorbid disorders, or have a higher risk for side effects with stimulant use (Banaschewski et al., 2004, Budur et al., 2005). Studies have indicated that these drugs have also resulted in behavioral improvement in individuals with ADHD (Biederman & Spencer, 2000). Some may reduce hyperactivity and impulsivity, comorbid aggression, tics, and moderate sleep disturbances (Banaschewski et al., 2004). According to Biederman and Spencer (2000), TCAs have been well tolerated and effective in regulating ADHD symptoms in studies with over 1,000 children. In addition, they also indicate that other non-stimulant medications, such as cholinergic drugs, may be helpful in

improving executive function in individuals with ADHD.

Despite the benefits of non-stimulant medications, it does have a few weaknesses. As with all medications, it does produce side effects, such as decreased appetite, dizziness, indigestion/nausea, fatigue/lethargy, irritability, drowsiness, and vomiting, among others (Weiss et al., 2010). Some children taking the non-stimulant atomoxetine have been found to experience psychiatric reactions such as changes in personality (Weiss et al., 2010). Also, according to a study by Abdulrahman and colleagues (2011), the poison control center receives an increasing amount of calls regarding adverse effects that occur in children receiving these medications. The calls ranged of severity from moderate to major effects that required hospitalizations and intensive care.

Other treatments include cognitive behavioral therapy, as well as parent based trainings. The use of cognitive behavior therapy (CBT) involves either a modular approach, or a case conceptualized orientation approach (Ramsay & Rostain, 2011). In the former approach, the individual learns about coping strategies (Safren et al., 2005) while personalized treatment plans are created for the individual in the latter (Ramsay, 2012). CBT treatment for ADHD has been demonstrated to have a positive effect. In a study conducted by Ramsay and Rostain (2011), 5 patients received CBT, and during the post-treatment phase, they found that ADHD symptoms were reduced. This form of treatment is beneficial for those individuals who refuse to or who are not able to take medications (Ramsay et al., 2011; Ramsay, 2012; Weiss et al., 2012). Although CBT seems to have a positive effect on symptoms, the effects of the therapy are best exhibited when accompanied by medications (Emilsson et al., 2011; So et al., 2007) making it difficult to

conclude that the active treatment is CBT and not the medications. Another issue with research on CBT is that most studies conducted using these strategies involve adults and adolescents (Ramsay et al., 2011; Ramsay, 2012; Safren et al., 2005; Weiss et al., 2012; Young et al., 2010), and do not focus on children. The fact that CBT treatments have not been extensively studied with children may be an indication that it is ineffective or that the cognitive piece cannot be accurately implemented in the treatment process given that children struggle with their ability to reflect on their own thoughts. This can be a huge issue given the importance of early intervention with this population to ensure a better prognosis and attempt to prevent the development of other comorbid conditions described above (Amiri et al., 2013; APA, 2013; Yoshimasu et al., 2012). Another issue is that research involving using CBT as a form of treatment in children is limited and outdated. According to a review study by Toplak and colleagues (2008), the latest research involving using CBT on children with ADHD was published in 1999. This study involved having an ADHD group and a control group use CBT strategies (i.e. guidance on effective strategies for improved performance, goal setting, problem solving) to improve on visual and auditory attention tasks. The study yielded positive results, with children developing an improvement on sustained attention in both tasks, but this study was conducted only on children with a less severe case of the disorder (Semrud-Clikeman et al., 1999).

Another non-pharmaceutical treatment used in the treatment of ADHD is parent based training. In parent based training, parents are trained to manage their child's behavior when disruptive or oppositional behaviors occur. In a review conducted by Power and colleagues (2002) they reported that the benefits of parent training include cost effectiveness, its effective

applicability in both children and adolescents across several domains of functioning, structured format and clear guidelines for implementation, and its social acceptability for parents and children. Also, a study by Danforth and colleagues (2003) found that group parent based training resulted in reduction of children's defiant, aggressive and hyperactive behaviors, and improved parent behavior and stress. Upon further examination of these parent-based models, many of the techniques appear to be behavioral in nature.

Despite the benefits of parent based training, there are several barriers that prevent parents from implementing training techniques, such as time constraints, knowledge regarding best practices, and multiple distractions from other caregivers or family members (Kazdin, 1997; Ortiz et al., 2013; Power et al., 2002). Ethical issues involving parent training have also been reviewed. Shevin (2001) examined a broad range of ethical concerns such as the constitution of proper targets for intervention and potential conflicts between parent and child rights, issues with positive contingencies and with the accepted use of punishment, conflicts between parents and researchers regarding the use of techniques, and the level of training the parents receive to design and implement the program on their child.

Given the barriers with parent training programs, one alternative is to identify and use a single behavioral treatment in symptom reduction. One possible treatment that may be effective in reducing hyperactivity in children is the use of physical activity. This may be a better treatment option given that these children eventually need to learn to implement treatment independently as they age. Studies have indicated that physical activity significantly reduced ADHD symptoms (Archer et al. 2012; Gapin et al. 2010; Gapin et al. 2011; Zivkovic et al.

2012).

For example, Gapin and Etnier (2010) investigated the role of physical activity on executive function. In this study the authors aimed to identify to what extent physical activity is associated with executive functioning in children with ADHD. Researchers measured subjects' moderate to vigorous physical activity using an accelerometer, which subjects wore on a daily basis, as well as a daily log that subjects recorded the types of physical activities they engaged in. Executive functioning was measured using several assessments. They measured inhibition, planning, working memory, and processing speed. Results of this study revealed that physical activity was significantly associated with planning.

In addition to the role that physical activity has on executive function, other studies indicate that physical activity may have an effect on behavioral symptoms commonly observed in individuals with ADHD. For example, Archer and Kostrzewa (2012) evaluated whether exercise can manage behavioral symptoms. They found that although research is limited, literature supports physical activity to alleviate a plethora of ADHD symptoms. In reviewing the literature they found regular exercise is beneficial against the effects of ADHD symptoms, stress, and some comorbid symptoms, including anxiety and depression. Also, Singh and colleagues (2010) surveyed participants who were diagnosed with ADHD regarding what strategies they thought was most helpful in managing the symptoms and the participants reported that engaging in physical activities or sports was the most helpful. Participants also mentioned that they believed physical activity along with stimulant medications would be more effective than physical activity alone.

Zivkovic and colleagues (2012) investigated physical activity in an attempt to reduce or

eliminate pharmaceutical treatment for this disorder. In this study, subjects engaged in kinezitherapy for 30 minutes, 3 times a week, for 3 months after diagnosis. Exercises implemented included warm up and attention training exercises where the children had to follow instructions provided. These exercises were implemented in a variety of settings. Physical activity was structured but also left some room for improvisation to allow for requests made by the children, but each session began with an organized routine. Results of this study presented a significant reduction in symptoms such as fidgeting, mumbling, excitability, inattention, failure to attend to tasks, "showing off," emotional impulsivity, rebelliousness, and non-cooperation. They also reported that parents noticed better attention spans, and reductions in the previously mentioned behaviors. Although, in a study conducted by Mckune and colleagues (2004), they concluded that their study is limited in that it is unclear whether the reduction of symptoms from their exercise program came from the attention subjects were given from exercise leaders and peers as opposed to the exercise program alone. The current study will control for many of these factors.

Despite the abundance of studies conducted in humans with ADHD, using human subjects can pose a variety of limitations and concerns. Issues may arise such as involvement of confounding variables and precision in the study, health issues the subjects may suffer from, and comorbidity in diagnosis. Studies involving humans have difficulty controlling for extraneous variables and the researcher's precision may impact the results of their studies. A number of variables could be intrusive in this line of research such as, medication, physical activity that may have occurred outside of the duration of data collection, attrition, or as previously mentioned, attention from researchers. Other issues that may interfere with studies in this area

include the child's health issues that might preclude their participation in these studies, such as asthma (Chen et al., 2013; Sleath et al., 2014), allergies (Chen et al., 2013), and obesity (Erhart et al., 2012; Lam & Yang, 2007), and comorbid disorders. An individual with ADHD and ODD whose parents agreed to participate in the study, may refuse to engage in any physical activity, or may influence others and impede the researcher's ability to gain compliance of other children to complete the physical activity required of the program. Using animals as subjects would prevent these issues and would make for a more controlled investigation of the impact of physical activity on ADHD symptoms.

Animal Models

There are a few models that have been established as animal models of ADHD. Strains include the Spontaneously Hypertensive Rat (SHR), with the Wistar Kyoto as the control, and the Lewis (LEW), as well as the genetically hypertensive (GH) with the Wistar as a control (Garcia et al., 2013). Most studies and literature reviews have been conducted on the SHR and its control (Genstch et al., 1987, Pardey et al., 2009, Sagvolden et al., 2009), with relatively fewer studies on the Lewis, GH, and its control (Garcia et al., 2013, Sutherland et al., 2009). This may be because the SHR model has been found to display all symptoms of ADHD, including inattentiveness, hyperactivity, and impulsivity (Pardey et al., 2008; Perry et al., 2010; Sagvolden et al., 2005; Sagvolden et al., 2009), when compared to the other strains. Sagvolden and colleagues (2005) found that the SHR is a valid model of ADHD because it fulfills the validation criteria for an appropriate animal model of the disorder. The authors proposed that an animal model of ADHD must conform to three validation criteria; face, construct, and predictive validity. Sagvolden and colleagues defined face validity as the ability to mimic the behavioral

clinical characteristics of ADHD. For example, behavioral clinical symptoms emitted by children with ADHD such as motor impulsiveness, deficiency in sustained attention, and hyperactivity must be modeled in the animal. Construct validity was defined as a theoretical rationale for the disorder. The rationale that was mentioned was that the rat must be a genetic model, display the structural and functional neuropathology of ADHD, have similar neurotransmitter dysfunction of dopamine and monoamine systems just as individuals with the disorder, it should display the same delay of reinforcement gradient as individuals with ADHD, display the behavioral characteristics, and display the same changes in neurobiological effects as those with ADHD if given psychostimulant medications. Predictive validity was defined as being able to predict previously unknown aspects of behavior, genetics, and neurobiology of the disorder from the model. These aspects with respect to SHR rats are, terms of more definite descriptions of altered delay gradient and emanate predictions of motor impulsiveness as the development of an surplus of responses with short IRT's, development of hyperactivity, and nature of sustained attention in ADHD. They later ran a study (Sagvolden et al., 2009) to determine the most appropriate control for the SHR. In this study they reviewed genetic and neurobiological data of the SHR rat by measuring genomic variation in animal models of ADHD, and confirmed that it is the proper strain as a model for combined type. Research conducted by Pardey and colleagues (2008) further supported SHR rats as an appropriate animal model for ADHD.

Given that research suggests that SHR rats are an appropriate animal model for ADHD, it is possible to use these rats in an experimental way to evaluate the effectiveness of various treatment options for ADHD. SHR rats have been used as the appropriate animal model of individuals with ADHD and many studies have evaluated the effects of pharmacotherapy as a

treatment for this disorder (Mook & Neuringer, 1993; Wickens et al., 2011). Wickens and colleagues examined how using animal models for ADHD is guiding clinical drug development. Researchers reviewed clinical features of ADHD and how they are used for laboratory study as well as the mechanisms used to have the animal model display ADHD like behaviors. They concluded that using animal models does show promise for future drug development.

As mentioned previously there are a few treatment options aside from pharmacotherapy for individuals with ADHD. Therapeutic treatments that have been explored include CBT and parent-training in humans, as mentioned above. However, these treatments have their own limitations and cannot been used with SHR rats. One treatment procedure that has been implemented with humans is the use of physical activity to reduce ADHD symptoms. However, these studies are limited in that they have confounding variables and difficulty with precision, subjects' health issues, and comorbidity of disorders. Increasing physical activity has also been applied to SHR rats to reduce ADHD behaviors in a few studies (Hoffman et al., 1987; Ko et al., 2013; Robinson et al., 2011).

For example, Hoffman and colleagues (1987) began this investigation with their study on the effect of voluntary exercise on open-field behavior and aggression in SHR rats. In this study, rats had free access to a running wheel for 42 days for the exception of the initial control period which lasted 16 days and a post control period which lasted 12 days. They ran an open-field test where activity was measured and an aggression test. During the open-field test which lasted 9 minutes, the running wheels were locked and activity such as home cage activity (where the rat would exit the home cage and cross areas within the open field cage) were measured. In the aggression test, which lasted 9 minutes as well, four randomly chosen rats, two controls and

two “runners,” were mixed and aggressive behaviors were measured. Aggressive behaviors were defined as attack, offensive upright posturing, and supine submissive posturing. They found that after 6 weeks of spontaneous running exercise, open-field activity and aggression were both reduced. In this experiment, SHR physical activity (i.e. the running wheel) was voluntary, which leaves some doubt as to whether rats actually engaged in the running task. Also, the rats used were adults during the time these procedures were carried out.

Robinson and colleagues (2011) also examined the effect of exercise on ADHD behaviors using SHR rats. Their study attempted to investigate the effects of voluntary wheel running during adolescence on attentional function. In the study, SHR rats were the exercise group and had free 24 hour access to a running wheel for the exception of a 1 hour period before behavioral training. The control group had no access to a running wheel. Unconditioned orienting behavior, conditioned responding of food cup behavior, and locomotor activity were measured. Unconditioned orienting behavior was monitored by breaks in photobeams mounted on the walls of the chamber during non-reinforced presentations of a light. They defined orienting as rearing on the hind legs with both forepaws off the ground. Conditioned food cup behavior was measured by breaks in the photo-beam located across the entry of the food cup during presentation of a light. Locomotion was measured by whether or not the rat crossed over a line drawn perpendicular to the long side of the tub on a video screen. Locomotor activity was measured using an open-field apparatus. The study indicated that both male and female SHRs that engaged in voluntary wheel running during their adolescent stage exhibited unconditioned orienting behaviors closer to that of their control during adulthood. This study indicates that physical exercise improves the attention-deficit symptom of ADHD in the SHR rat. This study

also had running as a voluntary procedure available to the animals which, as mentioned previously, the rats may or may have not used. The age of these rats was also a factor in this experiment because the rats were adolescents.

A study conducted by Ko and colleagues (2013) found that swimming, as a form of physical activity, had an effect on reduction of ADHD behaviors, as well. In this investigation, SHR's were forced to swim for 30 minutes once a day for 28 days, then put through a series of tests to measure hyperactivity, impulsivity, and aggressive and non-aggressive behaviors, and short-term memory. To measure hyperactivity, an open-field test was used. During open-field measures, rats were placed in the apparatus for six minutes. In the initial minute, the rat was allowed to explore freely before recording began, and in the 5 minutes that followed, open-field activity was recorded. This measure was scheduled at 9, 18, and 26 days following the beginning of the experiment. To measure impulsivity, a well-established apparatus called the Elevated Plus Maze test was used. This apparatus is used to measure anxiety in rats according to their aversion of the open space area in the maze. In this study, this measure was used, 28 days after the beginning of the experiment, the rat was placed in the center of the maze facing the open arm areas, and impulsivity was measured in accordance to the time spent in the open arms. This data was collected for 7 minutes. Aggressive and non-aggressive behaviors were measured using a social interaction test. Two weight-matched rats, a normal rat and a test rat, were selected and placed in the center of a test box. Interactions between the rats were recorded for 10 minutes. Non-aggressive behaviors were defined as genital investigation, sniffing, following and grooming. Aggressive behaviors were defined as kicking, boxing, biting, crawling over or under the partner, and touching the partner's face. Short-term memory was measured using the step-

through avoidance test. In this test, the rat is placed in an apparatus in which if it crosses into the dark compartment of the apparatus, they receive a shock. The latency of staying in the lighted compartment was measured 2 hours after the acquisition trial for a maximum of 5 minutes. Results indicated that after swimming exercise, there was suppression of all investigated symptoms. Although the physical activity in this experiment was not voluntary, the rats in this study were also adults. Also, SHR rats were given Atomoxetine as a form of treatment as well.

One commonality in these studies is that they all used adult rats. However, ADHD symptoms as mentioned earlier, manifest during childhood (APA, 2013), so using adult rats would not be representative of the child population. Another limitation is the researchers in most of these studies were providing physical activity as a voluntary task; whereas, if we are going to investigate its effectiveness in a treatment study, the rats should be required to engage in this behavior. As per findings from the previously mentioned studies, it is indicated that physical activity reduces ADHD symptoms in SHR rats. However, research regarding this topic is still lacking in that not many researchers have conducted studies regarding physical activity as a form of treatment in an animal model of ADHD. The current study will provide further investigation into this realm of research and contribute in hopes to include physical activity as one of the primary research based forms of alternative treatments for ADHD. In the following study, exercise was used as a behavioral treatment to reduce hyperactivity, one of the symptoms of ADHD, in an animal model.

CHAPTER II

METHODS AND PROCEDURES

Methods

Subjects

Four male Spontaneously Hypertensive Rats (SHR's) were used as experimental subjects, and four male Wistar Kyoto (WKY) rats were used as the control subjects. The animals were obtained from Charles River laboratories and were 21 days old. Weight of the rats was 41 to 42 grams. Rats were housed in pairs in plastic home cages (18" L X 8.1" H X 9.3" W) in a room located in the Behavioral Neuroscience Building. All rats were color coded for distinguishing purposes. A mark was made on their fur using non-toxic washable markers and was re-applied as needed. The animals had free access to food and water ad libitum while in their home cages. Weight, food, and water intake was monitored daily throughout the duration of the study.

Apparatus

This study will involve the use of two different apparatuses that will record different information regarding behaviors. The first apparatus was the running wheel and it was used to measure physical activity to ensure that the SHR rats are engaging in the physical exercise (i.e., running) required for this project. The other apparatus was the open field test and it was used to measure hyperactivity. Both of these apparatuses are described in detail below.

Wheel Running Task. A wheel running task was conducted using a running wheel (ENV-046) obtained by Med Associates Incorporated. The wheel features stainless steel grid rods and measures 8” in diameter and is attached to a plastic home cage that includes stainless steel rods above with an indentation that could be used as a food tray. A manual door is located between the home cage and the wheel 3” W X 4.5” H. An electronic brake control is also available and features nine preset resistance levels. The apparatus includes an LCD counter that is mounted alongside the wheel and displays the revolutions. A quarter of a wheel turn marks one revolution.

Open Field Test. The open field measure was conducted using an open field apparatus (ENV-515) obtained from Med Associates Incorporated. It encompasses a white open field area enclosed by four walls measuring 17” x 17” x 12”. The walls include three 16 beam adjustable IR strips that measure vertical activity, one located around the entire arena and two located on the side walls of the apparatus. The apparatus connects to a single computer that may hold eight open field stations at a time. The software that was used to record activity was the ENV-520 Activity Monitor. This software displays recorded activity the rat engaged in while in the apparatus, such as distance traveled, stereotype counts, vertical counts, average velocity, ambulatory counts, jump counts, and resting states.

Data Collection and Analysis

For the wheel running, data was collected by documenting the number of revolutions displayed by the counter connected to the running wheel after the rat has completed the allotted running duration. This number was plotted on a graph and the counter would be reset for the next rat. This was done for each of the SHR rats. WKY rats did not engage in wheel running. For the

open field test, the ENV-520 Activity Monitor software produced data on the number of squares the animal crosses for the allotted exploration time. This data was plotted and analyzed. This was done for both SHR and WKY rats and was conducted throughout the duration of both baseline and treatment phases.

Procedures

An ABAB reversal design was used for this experiment. In this within subjects design, a baseline of a behavior is collected until the behavior reaches a steady state, and then a treatment is implemented. This process is repeated for two more occasions to determine whether treatment has an effect on the targeted behavior. In this study, the animal's targeted behavior would be hyperactivity and the treatment would be running. To begin the study, the rats underwent a process of habituation to help them become more accustomed to the equipment and their new home. After the rats completed the habituation phase, a baseline was collected to determine the relative rates of hyperactivity of the SHR rats and WKY rats without being required to engage in physical activity (A). Baseline continued to be collected until hyperactivity reached a steady state. The SHR rats were then expected to engage in wheel running in the treatment phase (B).

Following this wheel running, they were placed in the open field arena to measure hyperactivity, this procedure was done throughout the study to obtain continuous measurement of hyperactivity during both baseline and treatment phases. Due to time constraints regarding maturation of the animals, the experiment was completed within the time of 3 months, at which stage rats reached the equivalent of a 9 year old human (Sengupta, 2013). This consisted of three baseline phases and three treatment phases. These procedures will be discussed in more detail below.

Habituation

A habituation procedure was conducted for each apparatus so that the animals may become familiarized with them. Habituation was implemented 2 days after obtaining the animals. Rats were first habituated to the running wheel for 15 minutes. SHR rats engaged in this procedure with the running wheel unlocked to habituate to the wheel, which was the treatment that was evaluated. The WKY rats engaged in this procedure with the wheel locked since they do not have to engage in wheel running and were the control group used for comparison. During this phase, the revolution counter on the running wheel was turned off since there is no need to document at this point. They were then placed in the center of the open field area and be allowed to explore for 15 minutes. After the 15 minutes, they were placed back in their home cages. The habituation procedure continued for 5 days.

Baseline (A)

Baseline data was taken for each rat using the open field task and wheel running to determine the animals' behavior in these tasks prior to treatment. This was conducted for both SHR and WKY rats. As mentioned prior, this study was an ABAB reversal design, so this procedure was implemented once more following the first wheel running task. All rats were in this phase for 10 days during the first baseline, and 5 days during the second and third baseline phases.

Wheel Running Task. During the baseline phase of the wheel running task, they were taken from their home cages and placed in the wheel. Once in the running wheel, the sliding door on the wheel was closed and the rat was forced to remain in the wheel. During the baseline phase, the wheel was locked for both SHR and WKY rats so that no wheel running took

place by both groups, but the wheel running environment is still being experienced. A timer was started to keep time of the 15 minute duration. After the 15 minutes they were placed back in their home cages. All rats were in this phase during baseline.

Resting Phase. After the wheel running task, rats were placed back in their home cages. This was done to provide them with the same experience they undergo during treatment.

Open Field. This procedure will follow the resting phase. Rats were taken from their home cages and placed in the lower left corner of the open field arena. They were allowed to explore for 10 minutes. After the allotted time, rats was taken out of the apparatus and placed back in their home cages. Both SHR and WKY rats engaged in this task. All rats underwent this procedure throughout the entire duration of the study.

Treatment (B)

Once a baseline was achieved, each rat underwent treatment. Wheel running was implemented as treatment and levels of hyperactivity in response to treatment was measured after wheel running using the open field test. Each treatment phase lasted 10 days. This phase will be explained in more detail below.

Wheel Running Task. During the treatment phase of the wheel running task, SHR rats were taken from their home cages and placed in the wheel. Once in the running wheel, the sliding door on the wheel was closed and the rat was forced to remain in the wheel. A timer was started to keep time. Rats were provided with the opportunity to run for a 15 minute duration before moving in to the resting phase. If during the 15 minute duration in the wheel, the rat does not run, the wheel was manually turned four revolutions (one full turn) so they continue

running. The WKY rats were also placed in the running wheel with the wheel locked and placed back into their home cages once they have completed the 15 minute duration. All rats should be in this phase for 10 days during treatment.

Resting Phase. Immediately after wheel running, all rats entered the resting phase. In this phase, rats were taken from the running wheel and placed back into their home cages for 10 minutes to reduce fatigue.

Open Field. This procedure followed the resting phase. Rats were taken from their home cages and placed in the lower left corner of the open field arena and were allowed to explore for 10 minutes. After the allotted time, rats were taken out of the apparatus and placed back in their home cages. Both SHR and WKY rats engaged in this task. All rats underwent this procedure throughout the entire duration of the study (i.e. for both baseline and treatment phases).

CHAPTER III

RESULTS

As mentioned earlier, an ABABAB design was used for this investigation. The following includes data collected on the execution of wheel running and open field behavior in both WKY and SHR groups.

Wheel Running

Appendix A Figure 1 displays wheel running for both WKY and SHR groups. Wheel running was at zero revolutions as wheels were locked for both WKY rats and SHR rats during baseline 1. In treatment 1, the wheel remained locked for WKY rats, and for SHR rats wheel running ranged from 460 to 1310 revolutions. Trends for wheel running in this treatment phase were stable. During baseline 2, wheels were locked for both WKY and SHR groups, no wheel running took place. In treatment 2, the wheel continued to remain locked for WKY rats, no running took place. For SHR rats, wheel running ranged from 538 to 1783 revolutions. The trends in this treatment phase remained stable with the exception of SHR 8 who started off at running the highest revolutions then dropped and was maintained. Baseline 3 shows wheels were locked for both groups; therefore, rats did not engage in running. For treatment 3, the wheel continued to be locked for WKY rats. For SHR rats, revolutions ranged from 573 to 1982 revolutions. The trend was highest in SHR 7, which peaked to the highest amount of revolutions on day 7 of this treatment phase then decreased and was maintained. There was a sharp increase in SHR 5 as well on the second day, but the next day it decreased and was maintained. Trends

were stable throughout treatment 3 for SHR 6 and SHR 8.

In Figure 2, the wheel running in baseline 1 was zero for both WKY 1 and SHR 5. For treatment 1, wheel remained locked for WKY 1. SHR 5 had a wheel running range between 719 and 1042 revolutions. The trend for this treatment phase was stable. No wheel running took place in each group during baseline 2. In treatment 2, SHR 5 wheel running ranged between 708 and 1107. The trend in treatment 2 was stable. WKY 1 did not engage in wheel running during this treatment phase. In baseline 3, there was no wheel running in both WKY and SHR 5. Treatment 3 presents a range in wheel running for SHR 5 of 721 to 1777 revolutions. There was a sharp increase in wheel running the second day of this treatment phase for SHR 5, but then it dropped and was maintained the next day. Wheel running for WKY 1 remained at zero.

Figure 3 displays wheel running in baseline 1 at zero for both WKY 2 and SHR 6. In treatment 1, wheel running ranged from 587 to 893 revolutions in SHR 6, while WKY 2 did not engage in any wheel running. The trend for treatment 1 was stable. In baseline 2, no wheel running took place for either rat. In treatment 2, SHR 6 engaged in a range of 747 to 937 revolutions of wheel running. During treatment 2, the trend was stable throughout. There was no wheel running in place for both rats during baseline 3. WKY 2 did not to engage in any wheel running in treatment 3, while SHR 6 had a wheel running range of 580 to 1090 revolutions. During this treatment phase, wheel running started off with frequent revolutions for the first four days, then dropped and were maintained.

Baseline 1 in Figure 4 presents no wheel running in WKY 3 and SHR 7. During treatment 2, this figure shows wheel running for WKY 3 remained at zero and for SHR 7 revolutions ranged from 758 to 1310. The trend for SHR 7 started off with a low amount of

revolutions, then increased on the third day, and was maintained. Baseline 2 consisted of no wheel running for each rat. In treatment 2, WKY 3 engaged in no wheel running and SHR 7 had a wheel running range of 844 to 1327 revolutions. The trend remained stable with the exception of a sharp increase in revolutions on the last day of treatment 2. Both rats had the wheel locked in baseline 3, no running took place. Treatment 3 exhibits WKY 3 remained at zero revolutions, while wheel running in SHR 7 ranged from 722 to 1982 revolutions. The trend was stable, but there was a sharp peak in wheel running on the seventh day of this treatment phase, which dropped and was maintained the next day.

WKY 4 and SHR 8 wheel running remained at zero in baseline 1, as presented in Figure 5. For treatment 1, WKY 4 did not run. Wheel running for SHR 8 ranged from 760 to 942 revolutions. The trend was stable throughout this treatment phase. No running took place in baseline 2 for both rats. There was no running for WKY 4 in treatment 2, and SHR 8 had a wheel running range of 538 to 1783 revolutions. SHR 8 started off with frequent revolutions on the first day of treatment, but then revolutions dropped the next day and were maintained. Wheel running started off at its highest the first day of this treatment phase, but then dropped the next day and was maintained throughout the rest of treatment 2. Wheel running reverted back to zero revolutions throughout the duration of baseline 3 for both WKY 4 and SHR 8. Treatment 3 demonstrates no wheel running for WKY 4, and wheel running for SHR 8 ranged between 590 and 948 revolutions. Trends for wheel running remained stable for treatment 3.

Open Field

Appendix B Figure 6 displays open field behavior for rats in both WKY and SHR groups.

Baseline 1 reveals distance traveled for the WKY group ranged from 31.88 cm to 1583 cm. In the SHR group distance traveled ranged between 1066.80 cm to 2927.67 cm. Trends during this baseline phase were stable for both groups. In treatment 1, WKY distance traveled ranged from 36.09 cm to 1546.64 cm and SHR distance traveled ranged from 474.20 cm to 2927.67 cm. Trends for both groups continued to remain stable in this treatment phase. Open field activity in WKY rats ranged from 85.1 cm to 867.88 cm for baseline 2. Trends for WKY group were low and stable. Trends of SHR group show activity increased in baseline 2, distance traveled was a range of 1256.32 cm to 3632.88 cm. For the Wistar control group in treatment 2, distance traveled measured in the open field activity apparatus ranged from 102.86 cm to 984.42 cm. Trends continued to remain low and stable. SHR group open field activity distance traveled had a range of 1740.03 cm to 3538.22 cm. Trends for SHR group in treatment 2 were stable. Baseline 3 shows WKY activity in the open field arena ranged from 116.64 cm to 1140.46 cm. Trends for WKY group remained stable. SHR rat distance traveled in baseline 3 averaged from 2041.23cm to 4769.79cm. Baseline 3 shows trends were stable in the SHR group. WKY rats had a distance traveled range of 0 cm to 854.06 cm in treatment 3, and SHR rats had a distance traveled range of 1778.56 cm to 3821.02 cm. Trends were stable for both groups. Open field activity of SHR group did not reach the equivalent of WKY control group open field behavior by the end of the study.

Figure 7 displays distance traveled for WKY 1 and SHR 5. WKY 1 distance traveled ranged between 31.88 cm to 1175.04 cm during baseline 1. SHR 5 traveled a range of 1813.61 cm to 2711.03 cm. Trends were stable for both groups. Treatment 1 shows there was a range of36.09 cm to 767.41 cm distance traveled for WKY 1. SHR 5 traveled between 474.2 cm to

2536.32 cm. Trends continued to remain stable for both rats during treatment as well. During baseline 2, a range of 85.1 cm to 728.61 cm was collected for WKY 1, and SHR 5 had a range of 2312.4 cm to 3200.89 cm distance traveled. Trends for both WKY 1 and SHR 5 were stable in baseline 2. In treatment 2, WKY 1 traveled a range of 102.86 cm to 811.68 cm, while SHR 5 traveled 2301.45 cm to 3538.22 cm. Trends for both groups continued to remain stable. Baseline 3 presents a range between 116.64 cm to 353.14 cm for WKY 1, and SHR 5 traveled a range between 3248.32 cm and 4769.79 cm. Stability in trend was maintained for both groups. Treatment 3 displays a range of 0 cm to 553.82 cm for WKY 1. For SHR 5, there is a range between 2466.76 cm to 3963.46 cm. Trends continued to be maintained. Distance traveled increased in SHR 5, and decreased in WKY 1.

Figure 8 shows data on WKY 2 and SHR 6. In baseline 1, WKY 2 distance traveled ranged from 53 cm to 1211.03 cm. The trend remained stable throughout the baseline 1 phase. SHR 6 distance ranged from 1585.19 cm to 2927.67 cm and the trend also remained stable in baseline. Treatment 1 displays distance traveled ranged between 146.78 cm to 875.78 cm for WKY 2, while SHR 6 had a range of distance traveled between 1164.42 cm and 2081.62 cm. Trends for both rats remained stable. Baseline 2 reads a range of 93.15 cm to 867.88 cm for WKY 1 in addition to a range of 2331.47 cm to 3632.88 cm for SHR rat 6. Stability in trends were maintained for both WKY 2 and SHR 6 in baseline 2. In treatment 2, WKY 2 distance traveled ranged from 138.28 cm to 619.80 cm and SHR 6 ranged from 2139.10 cm to 3443.08 cm. Trends remained stable for both rats in treatment 2. Baseline 3 presents a range of 253.80 cm to 510.20 cm distance traveled for WKY 2. For SHR 6, distance traveled was between 2617.60 cm to 4110.51 cm. Trends were stable in both WKY 2 and SHR 6 during baseline 3. Treatment 3

consists of a range between 233.86 cm and 591.81 cm for WKY 2 and 2376.29 cm to 3489.70 cm for SHR 6. Trends were maintained during this treatment phase. By the end of the study, there was an increase in distance traveled for SHR 6 and a decrease in WKY 2.

Figure 9 displays WKY 3 and SHR 7 data. Baseline 1 ranges between 275.40 cm to 1583.99 cm for WKY 3, and between 1578.71 cm to 2617.73 cm for SHR 7. The trend in this baseline was stable for both rats. Treatment 1 shows a range of 193.21 cm to 1546.64 cm for WKY 3. SHR 7 had a distance traveled range of 961.59 cm to 2063.28 cm. Trends were stable for both rats during treatment 1. For baseline 2, WKY 3 open field activity ranged from 100.20 cm to 612.34 cm, and SHR 7 open field activity ranged from 1256.32 to 3248.23 cm. The trend for WKY 3 remained stable; however, there was a sharp increase on day 3 for SHR 7, which then stabilized throughout the rest of baseline 2. In treatment 2, 214.38 cm to 984.92 cm was the range for WKY 3. For SHR 7, distance traveled ranged from 1810.40 cm to 2607.07 cm. The trend remained stable for both rats during treatment 2. During baseline 3, WKY rat traveled between a range of 354.91 cm to 1140.46 cm, and SHR 7 traveled a range of 2041.23 cm to 4399.42 cm. The trend was maintained; however, there was a sharp decrease in open field activity for SHR 7 on the last day of this baseline phase. Treatment 3 presents a range of 283.89 cm to 635.43 for WKY 3 and 1826.79 cm to 3821.02 cm for SHR 7. Trends were maintained for both rats throughout this treatment phase. In this pair, distance traveled increased for SHR 7, and decreased for WKY 3.

Figure 10 presents a range of 446.90 cm to 1521.28 cm for WKY 5 in baseline 1. SHR 8 distance traveled had a range of 1066.80 cm to 2109.36 cm. Trends were stable for both rats in baseline 1. In treatment 1, WKY 5 traveled a distance between 281.4 cm and 1433.71 cm, and

SHR 8 traveled between 897.44 cm and 2433.56 cm. Trend was stable for SHR 8, the trend in WKY 5 had a sharp increase in day 3 for WKY 5, which dropped the next day and was maintained. For baseline 2 the figure displays a range of 32.13 cm to 779.8 cm for WKY 5, and a range of 2128.21 cm 3050.55 cm for SHR 8. The trend was stable during baseline 2 for WKY 4, and for SHR 8 trend was stable for the exception of the third day where distance traveled increased slightly, then dropped the next day and was maintained. WKY 5 distance traveled ranged from 126.21 cm to 908.96 cm in treatment 2 while SHR 8 ranged from 1740.03 cm to 3080.47 cm. The trend was stable for both rats during treatment 2. The final baseline phase, baseline 3, shows a range 167.10 cm to 725.05 cm in WKY 5 and a range of 2220.28 cm to 4270.08 cm for SHR 8. During this baseline phase, open field activity began at a long length of distance traveled, then the trend decreased until it reached midway in the baseline phase, at which point length of distance traveled increased until the end of baseline 3. Treatment 3 presents ranges between 358.60 cm and 854.06 cm in WKY 5, and between 1778.56 cm and 3786.16 cm in SHR 8. In treatment 3, there was a downward trend until the sixth day where it increased slightly then was maintained for the rest of the treatment phase. By the end of data collection, there was an increase of distance traveled in SHR 8, and a decrease in WKY 4.

CHAPTER IV

DISCUSSION

This study was conducted with the goal of determining whether physical activity in the form of wheel running reduces hyperactivity in SHR rats. Overall, wheel running had very little effect on hyperactivity in the SHR rat. The SHR group experienced at or below a 25% reduction of hyperactivity throughout the duration of this study. Also, open field activity remained high in comparison to the WKY control group. The graph in figure 1 shows wheel running remained relatively stable for the SHR group. SHR 7 ran the most out of the SHR group. In figure 6, the graph shows open field activity increased in the SHR group, and reduced in the WKY group by the end of the study.

For this study, reduction of hyperactivity was not low enough to conclude wheel running reduced hyperactivity in SHR rats, especially in comparison to the WKY group. This is inconsistent with what Ko and colleagues (2013) found physical activity in the form of swimming alleviated ADHD behaviors including hyperactivity. These findings are also inconsistent with Hoffman and colleagues (1987), who found physical activity in the form of spontaneous running lowers open field activity. However, these findings are consistent to that of Robinson, Hopkins, and Bucci (2011) who found indicating the open field behavior of wheel running male SHR rats was lower than that of non-exercising male SHR rats, but still much higher than open field activity of WKY rats.

Although wheel running did not reduce hyperactivity, the older the SHR rats, the more

they would engage in other behaviors such as orienting, scratching, stalling, and grooming while in the running wheel, which interfered with the method of having the animal run in the wheel continuously. These behaviors model the description of inattention given by Sagvolden, and colleagues (2005; 2009), as well as Russel and colleagues (2005) in a few of their investigations of a proper animal model of ADHD. This may be the SHR version of the attention-deficit symptoms that individuals with ADHD experience. Research indicates that as children get older, inattention became a more prominent symptom of ADHD (Curchack-Lichtin et al., 2013). Hyperactivity increased as the rats aged as well, which is consistent with DSM-V diagnostic criteria in children (Dalsgaard et al., 2013; APA, 2013). The current study found there was more variability in the trends of open field behavior in the SHR group as opposed to trends of the WKY group. As the rats aged, there was consistent variability of open field behavior in SHR rats throughout data collection, and in the WKY rats open field behavior became more stable towards the end of the study. Dalsgaard and colleagues report that revisions to the DSM include age of onset as 7 to 12 years of age, which could explain the increase in hyperactivity and inattentive behaviors of the SHR rats, since the rats were the human age equivalency of approximately eight years.

Although this is a well-controlled study, it has some limitations. One limitation is that there was a change in the rats' diet during data collection, which could have affected their wheel running. Also, results may have differed if data had been collected when the rats were most active, such as during the night, or if the timer on the lights of the room they were held in had been adjusted to imitate night conditions at the time of data collection. Another limitation is that neurobiological aspects were not evaluated during the investigation and they may have affected

the trends observed with the aging process.

Future research should investigate the relationship between age and SHR hyperactivity, as well as hyperactivity in individuals with ADHD. Also, replication of this study could be conducted with a treadmill instead of a running wheel so that physical activity is consistent. Research could also explore the function of distraction behaviors mentioned earlier, and perhaps even go as far as finding prevention or consequent plans for rats that engage in these behaviors. In addition, future studies could also examine the effects of different types of physical activity on ADHD symptomology in the SHR rat, such as swimming, climbing, and jumping. This examination could be applied to a human study, by studying the effects of physical activity, such as cardio, yoga, or strength training in children with ADHD. The level of intensity of physical activity could be another variable that may play a role in hyperactivity symptoms. Investigations could also include neurobiological factors that could interfere in the treatment of ADHD behaviors. Impending research could analyze other forms of treatment for ADHD behaviors in humans and the SHR animal model. Last, it may be useful to consider whether physical activity is related to hyperactivity, and include other variables such as operant tasks to investigate attention or impulsivity using response withholding tasks or an elevated plus maze task.

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APPENDIX A

APPENDIX A

ABAB Reversal Design (Wheel Running)

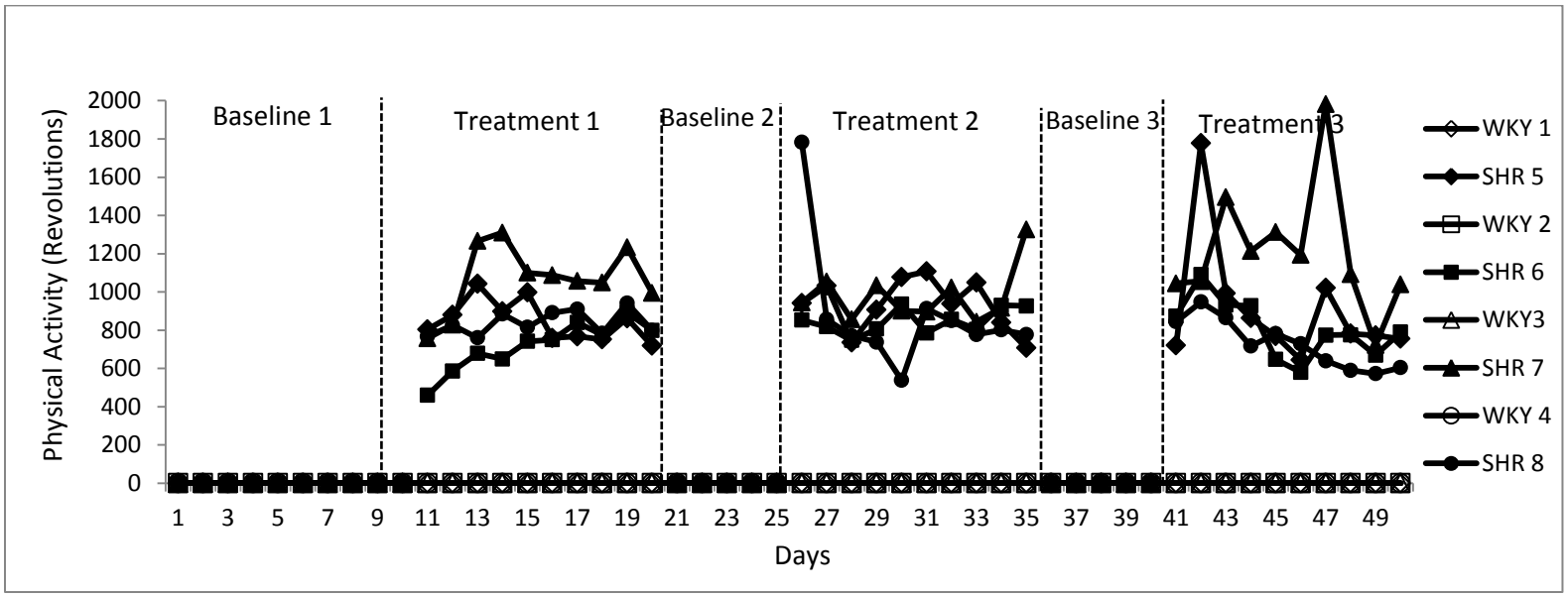

Fig. 1 Amount of Physical Activity per Day (WKY and SHR)

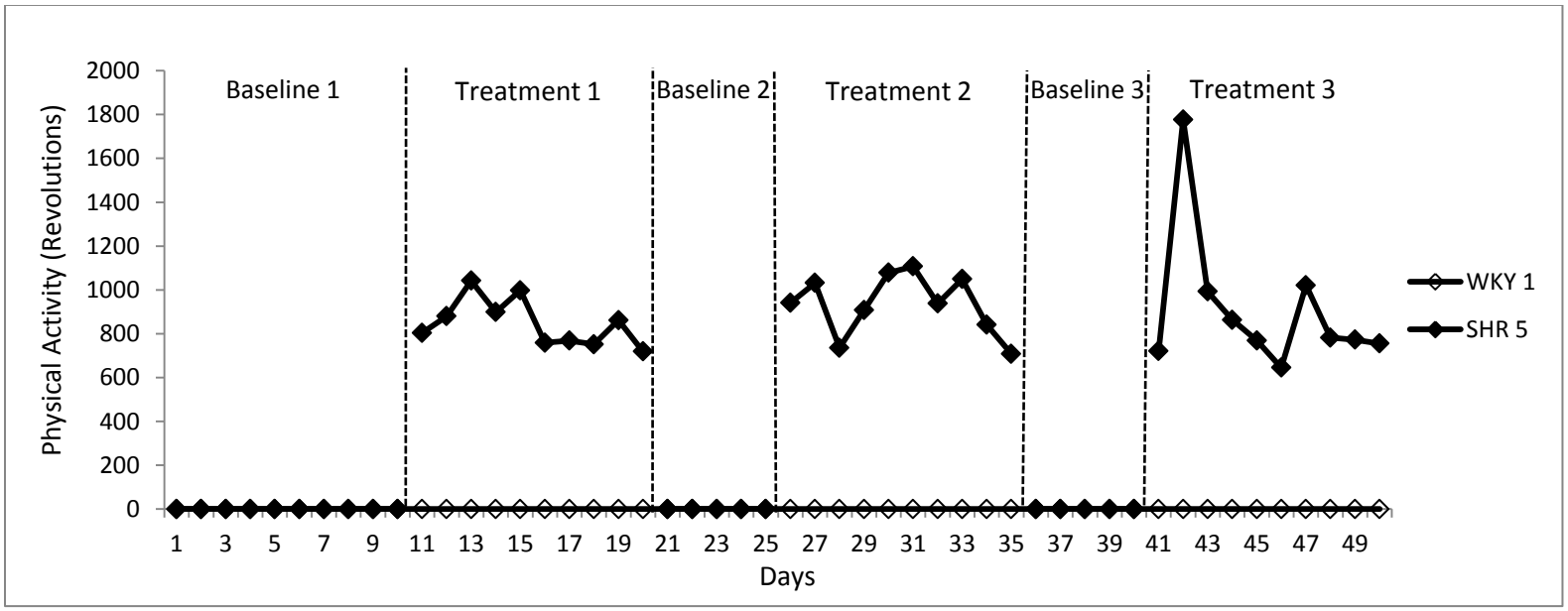

Fig. 2 Amount of Physical Activity per Day (WKY 1 and SHR 5)

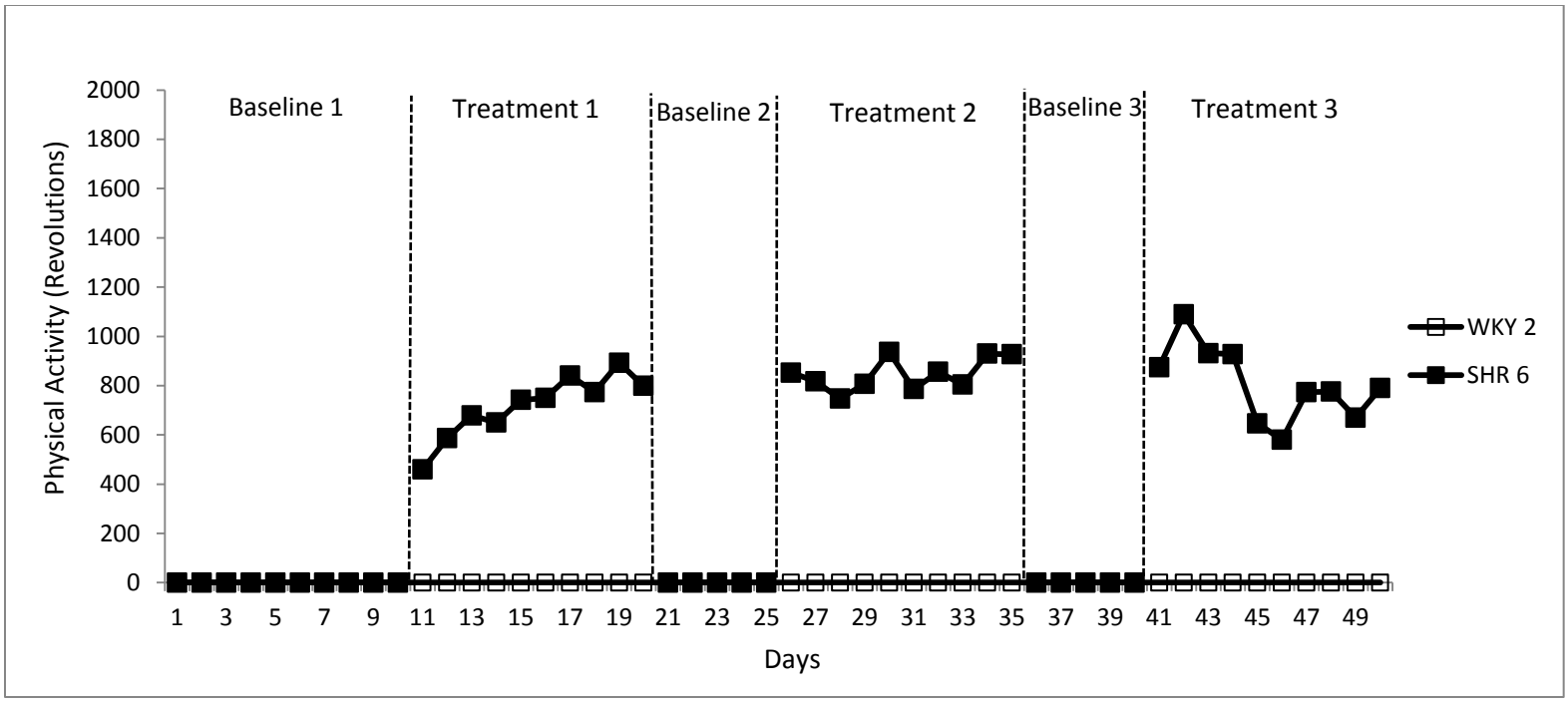

Fig. 3 Amount of Physical Activity per Day (WKY 2 and SHR 6)

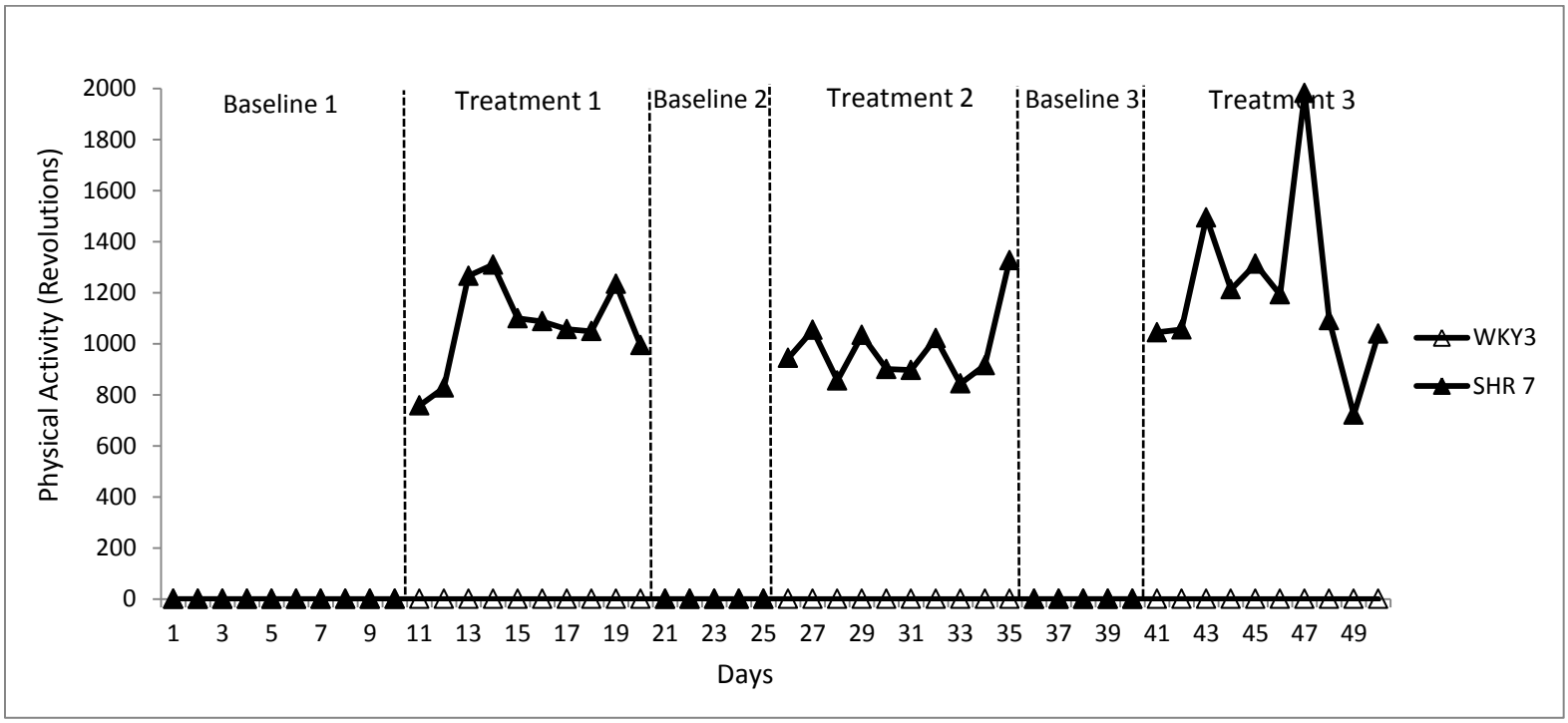

Fig. 4 Amount of Physical Activity per Day (WKY 3 and SHR 7)

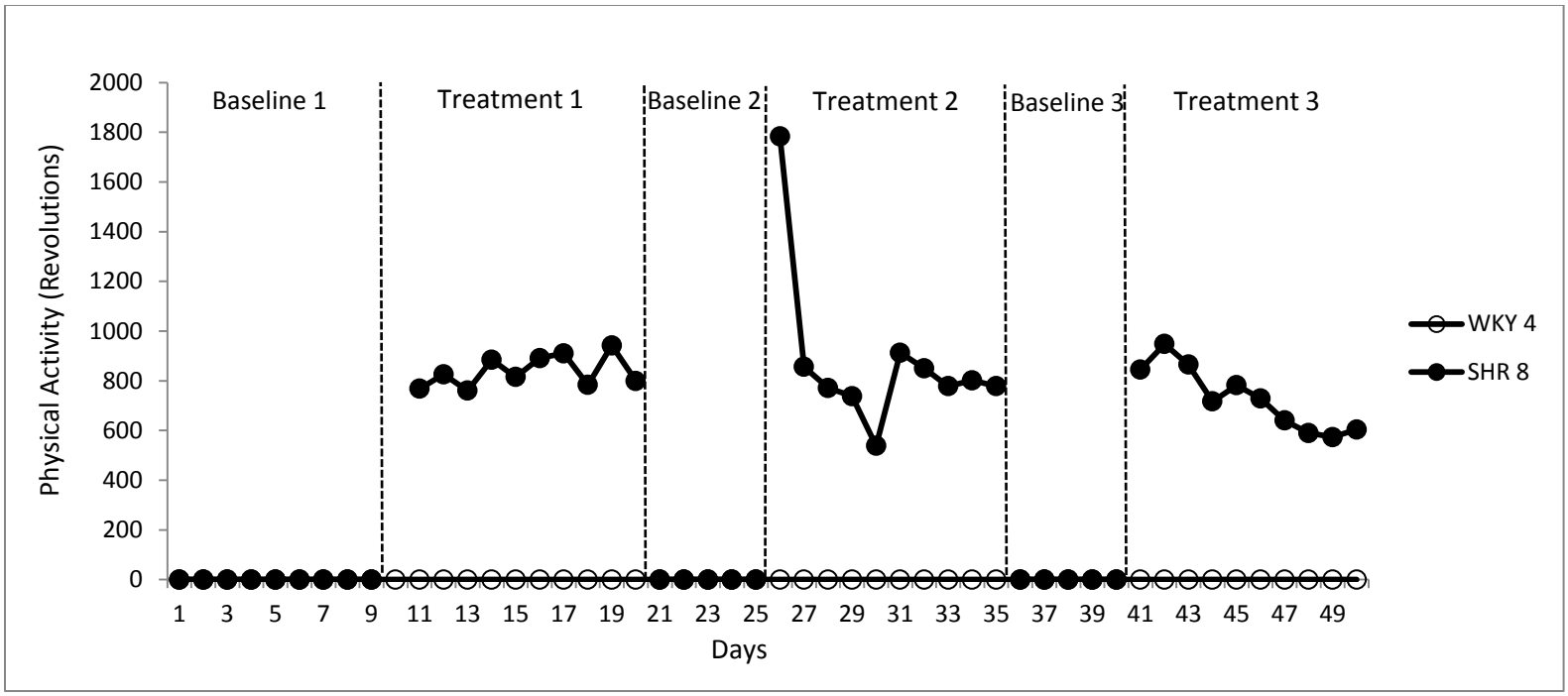

Fig. 5 Amount of Physical Activity per Day (WKY 4 and SHR 8)

APPENDIX B

APPENDIX B

ABAB Reversal Design (Open Field Activity)

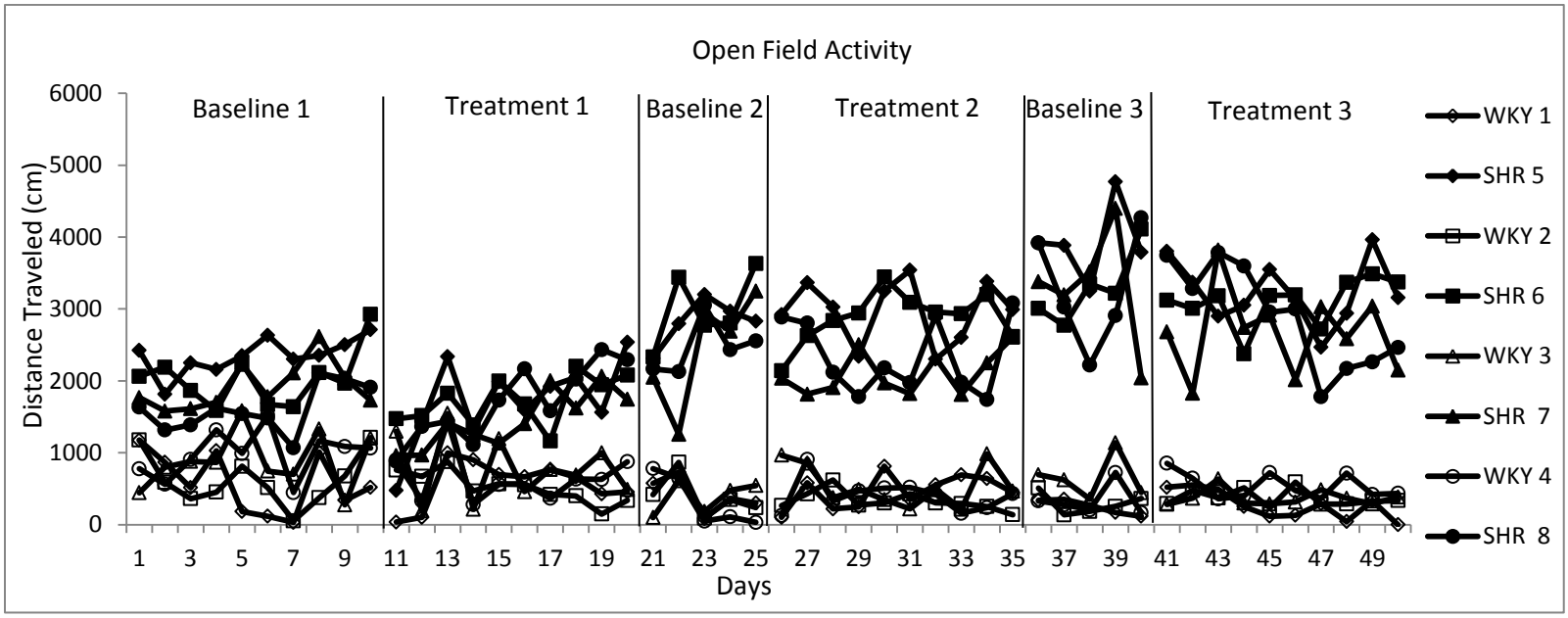

Fig. 6 Distance Traveled in Open Field per Day (WKY and SHR)

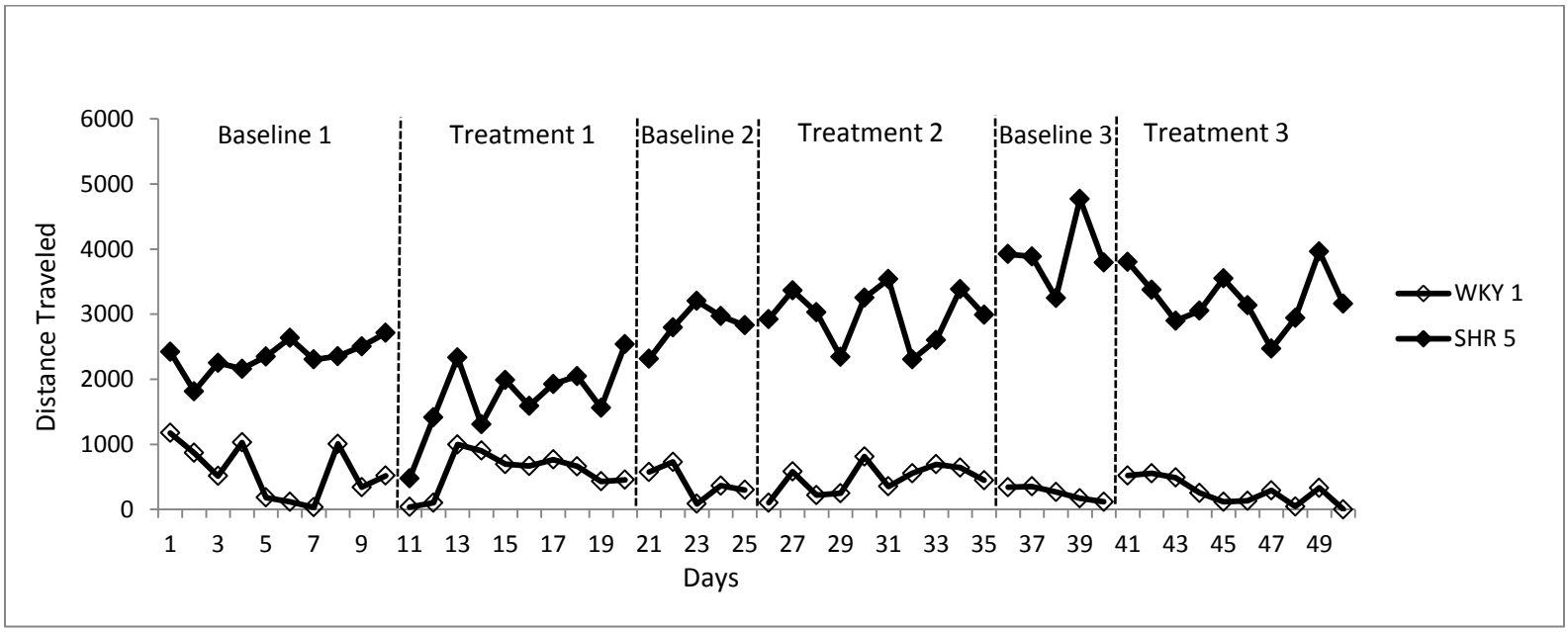

Fig. 7 Distance Traveled in Open Field per Day (WKY 1 and SHR 5)

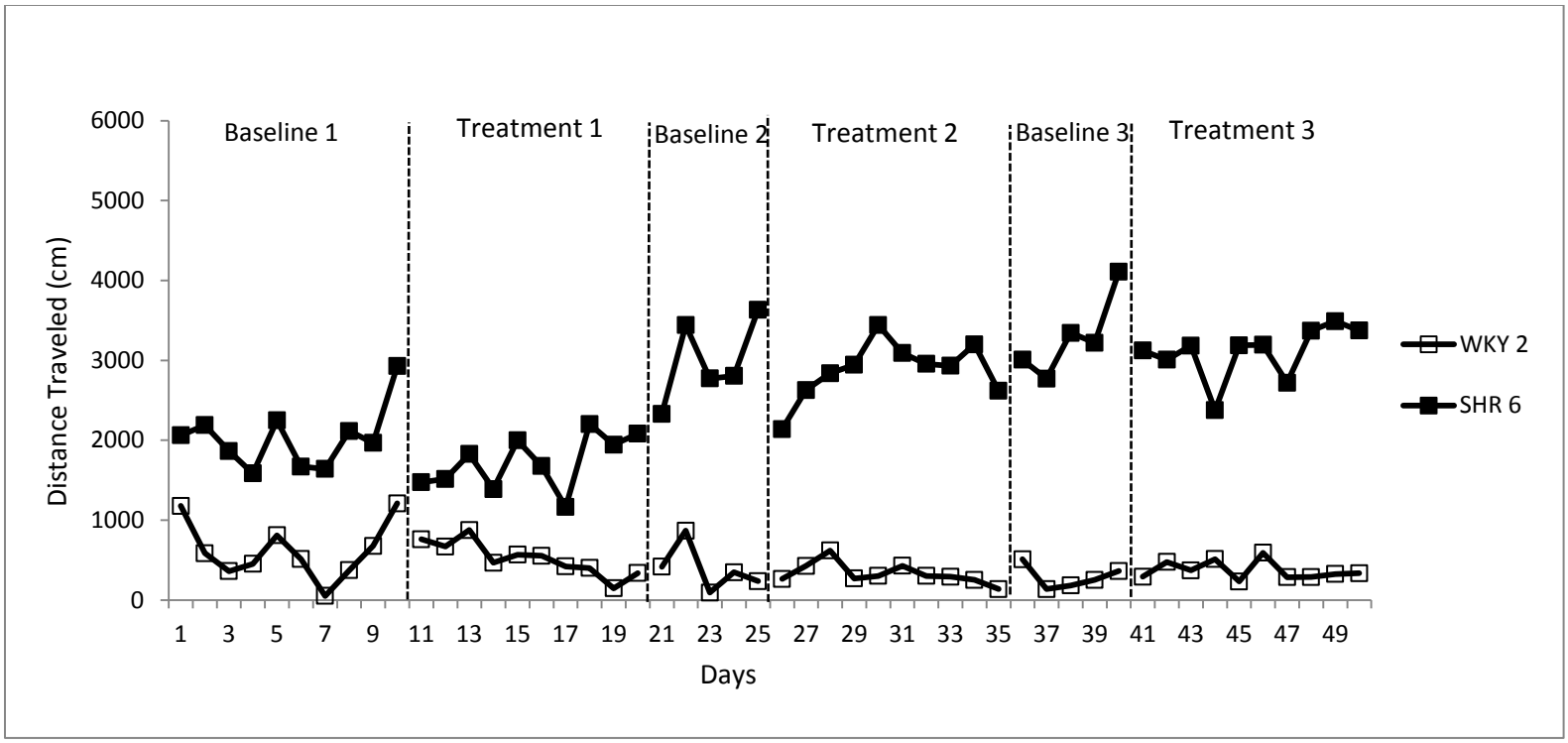

Fig. 8 Distance Traveled in Open Field per Day (WKY 2 and SHR 6)

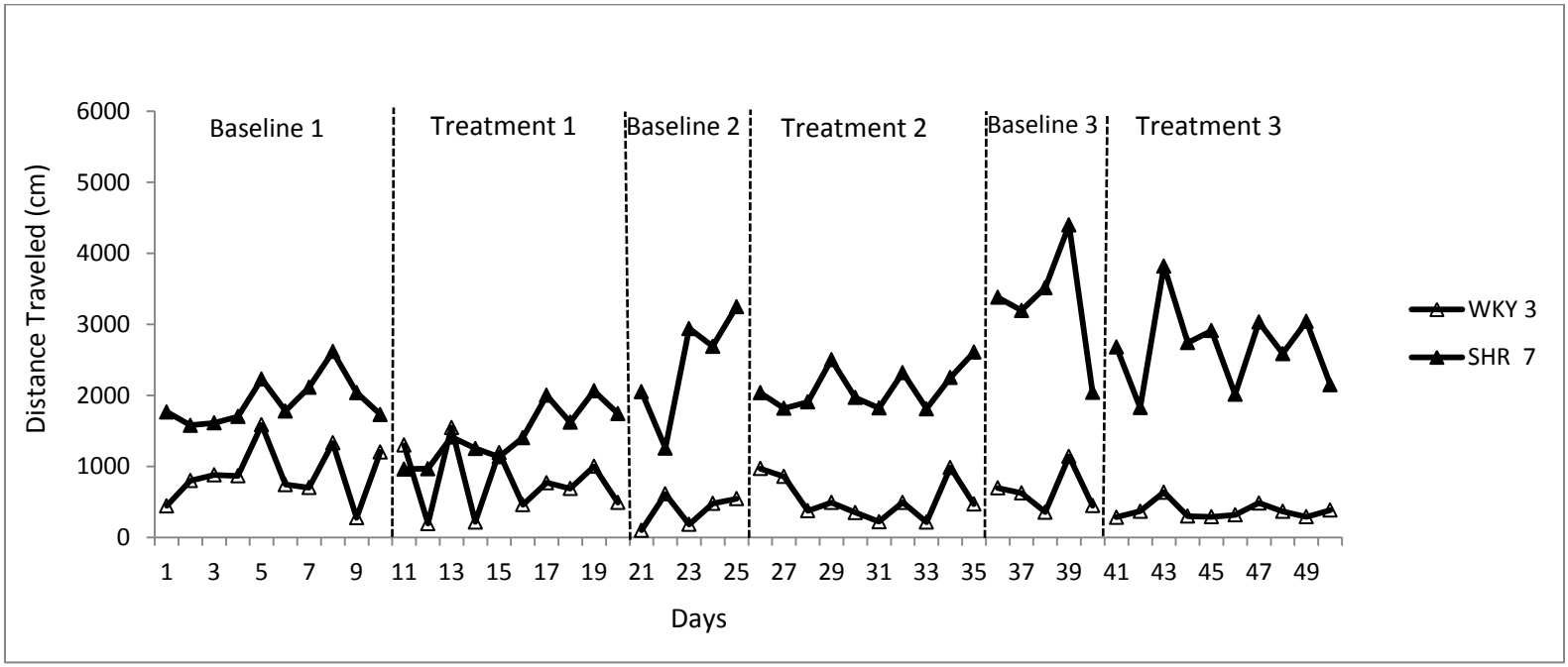

Fig. 9 Distance Traveled in Open Field per Day (WKY 3 and SHR 7)

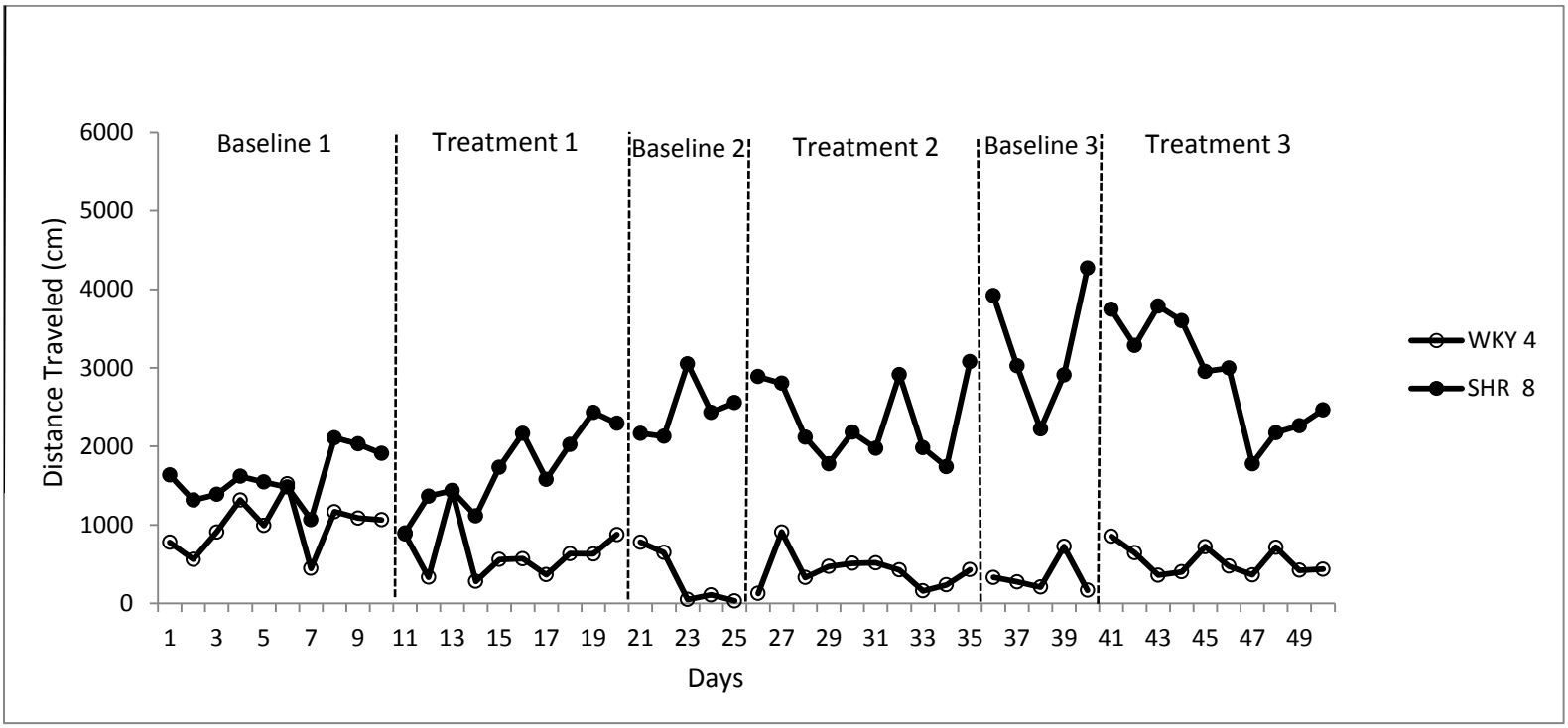

Fig. 10 Distance Traveled in Open Field per Day (WKY 4 and SHR 8)

BIOGRAPHICAL SKETCH

Jessica Martinez earned a Bachelor's degree in Psychology from the University of Texas-Pan American in December 2012. She joined the Masters program in Experimental Psychology in January 2013. In May 2015, she received a Master of Arts degree in Experimental Psychology with a concentration in Behavior Analysis. Ms. Martinez is a part of the Psi-Chi National Honor Society.

During her time as a Masters student as part of her hours of experience, Ms. Martinez was appointed to a few in-home programs centered on acquiring skills to work with children with Autism Spectrum Disorder (ASD). In addition, she gained some experience at a government state facility aside two board certified behavior analysts, Mr. Ruben Nieto and Ms. Berenice Martinez, assisting them with adults who have a wide range of psychological disorders and are housed in the facility. Ms. Martinez is currently continuing to gain experience with children with ASD by maintaining her work at an in-home program, and remaining an active participant in a non-profit organization called Team Mario that provides community based events for children with ASD.

Ms. Martinez has remained in the Pharr-San Juan-Alamo area throughout her educational career at the University of Texas-Pan American. She currently resides in Alamo, Texas with her Fiancé.