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Neurodevelopmental Basis of Autism Spectrum Disorder based on Age and Gender

Sursatie Chetram
Walden University

Walden University

College of Social and Behavioral Sciences

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Sursatie Chetram

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Review Committee
Dr. Jay Greiner, Committee Chairperson, Psychology Faculty
Dr. Christos Constantinidis, Committee Member, Psychology Faculty
Dr. Bonnie Nastasi, University Reviewer, Psychology Faculty

Chief Academic Officer
Eric Riedel, Ph.D.

Walden University
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Abstract

Neurodevelopmental Basis of Autism Spectrum Disorder based on Age and Gender

by

Sursatie D. Chetram

MA, University of New Haven, 2000

BA, Hunter, CUNY, 1997

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that affects communication, socialization, and restricted/repetitive behaviors. In 2012, one out of every 55 children (1 in 42 boys and 1 in 189 girls) have been diagnosed with ASD in the United States. Only 30-40% of ASD has a known etiology (e.g., genetic predisposition) and the other 60-70% is unknown. Prior to this study, there was no known literature on age and gender differences related to neuro-developmental functioning of ASD. The purpose of this study was to examine how the differences in age and gender of people with ASD were related to total and domain scores, as measured by the *Autism Diagnostic Observation Schedule, Second Edition* (ADOS-2). This quantitative research study included a sample size of 80 and 2 independent variables: age groupings (ages 1-4, 5-8, 9-17, and 18-older), and gender (male and female). The 4 dependent variables were the total and domain scores measured by the ADOS-2. The statistical analyses included a multiple analysis of variance (MANOVA) and a 2-way analysis of variance (ANOVA) to examine age and gender differences in the ADOS-2 domain and total scores. There was a statistically significant difference for age on the domain dependent variables, $F(9, 171) = 2.64$, $p = .007$; Wilks' Lambda = .73; partial $\eta^2 = .10$. However, there were no statistically significant differences for gender on domain scores and there were no statistically significant differences for age and gender on the overall scores. Those with ASD between ages 5-8 were more severely impaired for socialization when compared to other age groups and other domains. This research can be used for the improvement of intervention strategies for the diverse ASD population, and to improve the understanding of the neurodevelopmental functioning of individuals with ASD based on age and gender.

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Dedication

This paper is dedicated to my children for the sacrifice they endured while I took time away from them to focus on this journey. This is for you, Shaya, my sweet pea and, Laeko, my luv bug.Without the support of my mother and husband, this venture would not have been possible. This paper is also dedicated to my Mai for being my biggest inspiration. I would like to also dedicate this study to all autistic individuals, including my nephew, Kevin.

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I would like to thank my children for their love and support. Thank you for the many sacrifices you endured during this pursuit. I am forever grateful to you for your patience and understanding during this process. Thanks to my mom for supporting us in order to make this process possible.

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Chapter 1: Introduction to the Study

This was a comparative study between age and gender, and the neurodevelopmental functioning of autism spectrum disorder (ASD). The problem leading to this study stemmed from the unknown nature of ASD. According to the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5), ASD is a lifelong neurodevelopmental disorder associated with deficits in social affect (communication and social interaction), and restricted/repetitive behavior (American Psychiatric Association [APA], 2013). According to the *Autism and Developmental Disorder Monitor* (ADDM), one in every 55 individuals in the United States was diagnosed with ASD (ADDM, 2012). Furthermore, the ASD population was also gender-disproportionate: one in 42 were boys, while one in 189 were girls. The etiology of ASD was considered to be 30-40% genetic (Schaefer, 2016). However, there was no knowncause.

The problem leading to this current study was the lack of a known cause for 60-70% of ASD diagnoses (Schaefer, 2016). Researchers have conclusively demonstrated a link between age and gender, and the neurodevelopment component of ASD, using the ADOS-2. There were no studies available on neurodevelopmental differences based on age and gender when comparing the diverse groups of disorders within the autistic spectrum.

The gap in literature was that there was no research directly linking age and gender to the neurodevelopmental functioning of ASD. However, there was related research similar to age- and gender-based studies of ASD. Most of the literature review exhibited inconsistencies regarding the age and gender differences of people with ASD.

The inconsistencies were that some researchers found significant age and gender differences and other researchers did not indicate statistically significant differences. The inconsistent findings regarding age and gender were not directly related to neurodevelopmental functioning of individuals with ASD. The common themes in the ASD literature based on age and gender weredelays in testing, diagnosing and treating ASD (Daniels & Mandell, 2013). Rutherford et al. (2016) noted that the biggest factor in the delay of diagnosing ASD was associated with the age at which individuals were tested, diagnosed, and treated.

Commonly, individuals with ASD are not tested until at least their school age years. Delay in diagnosing could impact the critical, time sensitive during childhood developmental period. Furthermore, researchers did not identify gender differences in the research (Wilson et al., 2016). Wilson et al. reported that gender differences were a contributing factor to delay in testing. This delay resulted in "different manifestations of ASD phenotype," which may be due to the influence of the different responses of boys and girls as they age.

In this study, I demonstrated an age difference in the neuro-developmental components of ASD as measured by the ADOS-2. The purpose of this current study was to examine how the differences in age and gender of people with ASD were related to total scores and domain scores of communication, socialization, and restricted/repetitive behaviors of ASD when measured by the ADOS-2 (Lord et al., 2012). In this study, I demonstrated how differences in age and gender are related to the total (i.e., severity) scores and domain scores. I also examined possible differences between the four age groups of ASD participants.

I proposed that severity (total scores) and domain scores played a role in the differences between the four age groups. I further explored if impairments demonstrated by total and domain scores varied in importance according to age and examined differences in performance by gender. In addition, severity and domain scores were looked at to determine differences based on gender. I further sought to understand if men were more severely impaired than women, or vice versa. Domain component scores were determined during the study and I addressed gender difference in performance.

This was a quantitative study using a comparative analysis. The instrument used was the ADOS-2. There were four dependent variables (DVs) and two independent variables (IVs). The four dependent variables were the total scores and three levels of domain component scores. The three domain component scores were communication, socialization and repetitive/restricted behaviors of the ADOS-2. The independent variables were age and gender. The first independent variable was age of ASD participants, and subdivided into four levels: 1-4, 5-8, 9-17, and 18 years and older. The second independent variable was gender with two levels: male and female.

I conducted the statistical analysis with a MANOVA to test for the differences and relationships of age and gender on domain scores of the ADOS-2. I used the 2-way ANOVA to examine the relationship between age and gender, and total scores of the ADOS-2. I focused on a sample of ASD children, youth, and adults; the sample size was 80. Children were considered to be 8 years old and under. Youths were defined as between the ages of 9 and 17. Adults were age 18 and older.

ASD prevalence (see Appendix B) has more than doubled in the last decade, according to the *Autism and Developmental Disorder Monitor* ([ADDM], 2014).

According to the ADDM, in 2002, one in 150 individuals were diagnosed with ASD in the United States and other, similar industrialized countries. In 2010, the ADDM reported that one in every 68 individuals were diagnosed with ASD. The ADDM (2016) then cited a finding from the Centers for Disease Control and Prevention ([CDC], 2016) that 1 in 55 children had ASD. ADDM (2016) also reported that boys were 4.7 times more likely than girls to have ASD. There were no statistically significant differences for ASD in the United States among Blacks, Whites, or Hispanics. Saey (2010) reported that 10% of ASD was due to genetic factors and the other 90% had no known cause. However, Schaefer (2016) reported that the genetic factor of ASD increased to 30-40%. There seemed to be an upward trend for the genetic link to ASD. I based this study on the neuro-developmental aspect of ASD and considered all disorders across the ASD spectrum.

According to brain-based behavioral theory, ASD could be due to a dysfunction in brain operation, such as abnormalities, brain injuries, trauma or tumors(Weaver, 2015). Brain distortions could impact a specific region of the brain resulting in behaviors similar to ASD symptoms, which—as previously noted—affect socialization, communication, and restricted/ repetitive behaviors. The region most intensively studied is the intrinsic connectivity network (ICN) that impacts the neural network of the brain and can cause symptoms of ASD (Zielinski et al., 2012).

Impacts to brain functioning, due to injury or abnormalities could be associated with different regions of the brain, often result in impairments to one or more of the following functions: cognition, social functioning, and sensory/repetitive stereotypical behaviors (Chevignard, Catroppa, Galvin, & Anderson 2010). These impairments have

some similarities to brain injury (BI) and ASD (Radice-Neumann, Zupan, Babbage, & Willer, 2007). Brain distortion affecting functionality has been implicated in ASD, and may have a relationship to the level of functioning, age and gender, and brain functioning in ASD.

Scholars may use the results of this to affect social change by advancing research and intervention related to age and gender, based on neurodevelopmental functioning of individuals with ASD. The purpose of this study was to explore age and gender differences, which also showed that the level of severity (based on total scores) was related to age and gender. Also, another positive finding was that I provided researchers with information they can use to further develop programs and treatments in the field of ASD based on age and gender differences.

Background

The origin of autism disorder was found by Kanner (1943), who first theorized the existence of autism in the 1940s and coined the term *early infantile autism*. Kanner's first reference to autism concerned abnormal behavior noticeable in early infancy. From data collected by Pollack (1958), 30% to 40% of children with autism have mental retardation. Creak (1961) claimed that these children were ineducable (Edelson, 2006), and had serious mental retardation and childhood schizophrenia. At the time, childhood schizophrenia and childhood psychosis were used to identity autism. In the 1970s, increased research focusing on autism began to raise awareness and knowledge on the subject (DeMyer, Hingten, & Jackson, 1981). Yet, during this period, researchers often used terms such as *childhood schizophrenia* and *psychosis* for most childhood mental health and developmental disorders.

Kanner's (1940) theory of autism was based on impairments of specific functions, which had some similarities to current *DSM-5* diagnostic criteria of ASD. Again, these limitations were in the areas of communication, social interaction and restricted/repetitive stereotypical behaviors (APA, 2013). In 1940, Kanner first defined the disorder as the Kanner Syndrome, or autism disorder. He created the term early infantile autism to differentiate these symptoms from schizophrenia. He also indicated that autism would be noticeable during early infancy by its abnormal behavior. Kanner (1943) had an extensive list of features for the autistic syndrome.

Some of Kanner's initial key features were adopted and modified for the diagnostic criteria used in various revisions of the *DSM*. However, Kanner's (1943) list of symptoms was far more extensive than *DSM-5* criteria for ASD. Kanner's criteria were: (a) feeding problems since birth; (b) non-anticipatory posturing for pickup at four months old; (c) making peculiar loud noises and sensitivity to loud sounds; (d) repetitious language, behavior, and impulsive activity; (e) communication problems such as speech problems and non-verbalizations; (f) socialization problems such as the inability to relate to others, but attached to objects; (g) limited verbal ability while possessing an excellent rote memory for words, numbers and rhymes while also demonstrating good cognitive potentials; (h) appearing intelligent and serious minded; (i) physical normality; and (j) being born of intelligent families (Chambers, 1969).

The *DSM-III* (1980) classified infantile autism as a pervasive developmental disorder (APA, 1980). In the 1990s and 2000s, discussion of autism became prevalent. During this time, autism research exploded. Investigators and other experts developed more effective diagnostic tools and programs for autism. This led to the differential

diagnosis of Asperger, which had also been misdiagnosed for many years. Misdiagnosis was due to many factors, but primarily because of inadequate research funding. As is so often the case, a lack of funding limits meaningful research, which impacts access and availability to diagnostic tools.

The 2000s saw the beginning of an international rise in empirical research to identify the etiology of autism. The research in the ASD field expanded drastically in many areas, such as psychiatry, psychology, medical health, public health and social services. So far there was only one field that could clearly identify a known cause of autism, which was the genetic basis of autism. Although there may have been some research on autism as it related to neuro-developmental components of ASD, no definite link yet existed.

Problem Statement

The problem I addressed in this current study was that no known cause had been identified for 60-70% of the ASD population. Genetic factors account for 30-40% of the etiology of autism (Schaefer, 2016). To date, though, there is no known cause for the remaining ASD cases. The CDC (2016) showed that 1 in 55 children had ASD but, absent a clear etiology, the factors that determined the severity of the condition are far less understood.

There were numerous studies conducted on the involvement of age and gender on ASD. However, researchers revealed inconsistent findings on the impact of these difference on ASD (Daniel & Mandell, 2013). Thus, there was a need for this study. There were no known research studies directly addressing age and gender differences in the neuro-developmental functioning for those with ASD, as measured by the ADOS-2.

My objective in this study was to investigate if a relationship between age and gender and total scores and domain scores, as measured by the ADOS-2 existed.

Purpose of Research

The purpose of this current study was to examine how differences in age, and gender are related to total scores and domain scores for communication, socialization and restricted/ repetitive behaviors of ASD, as measured by the ADOS-2. I investigated the differences in neurodevelopmental functioning based on age and gender with participants within the autistic spectrum. What was known for differences in age and gender for the ASD population was reinforced. I also explored how the domain component scores reflected differences in age and gender. Also, I addressed how impairments, as measured by severity, varied between the age groups and genders.

A comparative research design and archival data were used. I measured the total and domain scores with the ADOS-2. The ADOS-2 is a standardized ASD instrument which is observationally based. Total score was the dependent variable and was also used as the severity indicator. Domain scores were also dependent variables and had the subscales of communication, socialization, and restricted/repetitive behaviors. As noted above, I used a MANOVA and a 2-way ANOVA for the statistical analysis of data. These tests were used to examine the relationship between age and gender, and that of the total and domain scores. The two independent variables were age (four levels) and gender (two levels). The four dependent variables were total scoreand domain scores.

Research Questions and Hypotheses

The hypotheses and the research questions for this study are:

Research Question 1

Are there age and gender differences in ADOS-2 domain scores of socialization, communication, and repetitive/restricted behavior?

$H_0$1: ADOS-2 domain scores of socialization, communication and repetitive/restricted behavior do not differ by age (categorical variable; ages 1-4, 5-8, 9-17, 18 and older) and gender.

$H_1$1: ADOS-2 domain scores of socialization, communication and repetitive/restricted behavior differ by age (categorical variable; ages 1-4, 5-8, 9-17, 18 and older) and gender.

The MANOVA test will be used for analysis.

Research Question 2

Are there age and gender differences in the ADOS-2 total scores?

$H_0$2: The ADOS-2 total scores do not differ based on age and gender.

$H_1$2: The ADOS-2 total scores differ based on age and gender.

The 2-Way ANOVA test will be used for analysis.

Theoretical Framework

The theoretical framework adopted for this current study was based on Zielinski et al.'s (2012) approach to the neurobiological basis of impairments found in ASD based on age, gender and IQ. These researchers provided evidence of disruptions in brain neural network architecture that underlie the behaviors of communication and socialization in ASD. The brain neural network architecture comprised of the intrinsic connectivity network (ICN), which consists of salience networks (SN) and default-mode networks (DMN).

The ICN components (SN and DMN) are involved with the clinical manifestations of autism (Zielinski et al., 2012). The SN is responsible for regulating social-emotional environmental stimuli, which is found to be restricted in autism. The DMN is involved in the abnormal engagement in cognitive processing and communication in autism. Zielinski et al. focused on the disruptions found in the brain's neural architecture, which impacts brain structures and functions in ASD. Zielinski et al.'s findings suggested decreased neural connectivity between SN nodes and increased connectivity within and outside the DMN. Their research showed distinct neural disruptions in younger autistics males (ages 3.49-22.33 years), suggesting neural network involvement, including the SN and DMN. Based on their study of these male autistic patients, neural disruptions found on brain structures could impact neuro-developmental functioning of individuals with ASD.

Nature of Study

This current study had 80 participants. Data werecollected from the National Institute of Mental Health – National Database of Autism Research (NIMH-NDAR) database. I initially selected particpants non-randomly because they were diagnosed with ASD using the ADOS-2 assessment. Next, I divided participants non-randomly into age groups. Within each age category, participants were selected randomly by gender. At this random selection stage, a 'five on' and 'five off' process was used. That is, five males were chosen, then skipped as the other five entries. Five more males were chosen again until the desired number of male participants was reached. The same selection process was used for female participants.

Participants were then selected randomly from an ASD-ADOS-2 pool composed of females and males, and children, adolescents, and adults. They were then placed in their respectively groups by age and gender. For gender selection, they were placed either in male or female groups. For the age groups, participants were placed according to age range (1-4, 5-8, 9-17, and 18+ years). Archival or pre-existing data were used for the DV scores. The ADOS-2 instrument was already administered to the ASD population for the DV scores. I chose the NIMH for data, which had already approved the data collection process for this study. NIMH stores ADOS-2 scores collected from other ASD-related research. The archival data collected from NIMH were the ASD diagnostic information, ADOS-2 scores, age, and gender. I used the ADOS-2 test scores, specifically the overall total scores and the domain scores, for this study.

Research Design

This study had a quantitative research design that I used archival data with a sample size of 80. The IVs were age and gender. The two independent variables had four levels of age and two levels of gender. The ages were 1-4, 5-8, 9-17 and, 18+ years. Genders were female and male. The four DVs were domain and total scores from the ADOS-2. There were 10 participants (p) per group of ages (a), and two groups of gender (g), which equaled 80 participants. The participants' formula was therefore, $n = (10p \times 4a) \times 2g$.

Archival data were from NIMH using the NDAR data set. Data collected were from ASD populations. NIMH-NDAR and Walden University's Institutional Review Board (IRB) approved the data collection previously. The data collected were obtained from NDAR records accessed from ASD participants. The data consisted of ADOS-2

scores, ASD diagnostic information, and demographic information (i.e., age and gender). This information was collected, analyzed, and reported (Chevignard et al., 2010).

Population and Data Collection

The researcher selected participants based on an existing diagnosis of autism. Participants were selected non-randomly and randomly in two phases. In the first phase, I selected participants non-randomly from a sample pool of ASD-ADOS-2-diagnosed clients from the NDAR database. I then further categorized them non-randomly by age groups. After that, the participants were randomly selected by gender from the same NDAR pool of ASD-ADOS-2 potential participants.

The sample population consisted of participants tested using the ADOS-2 neuro-psychological assessment. Archival data was the preferred method of data collection for this study. The target number of participants was 80 with an $\alpha = .05$, statistical power = .99, and a medium effect size of $f = .50$. The effective size was based on an average of three studies done on ASD population with children and adults. However, within each category, I randomly selected participants for gender, but the age and diagnoses groups were non-randomly selected, as detailed by Creswell (2009).

Operational Definitions

Autism: An early childhood neurodevelopmental disorder, which could also be fully manifested later in life (APA, 2013). Symptoms of ASD are exhibited by deficits in social communication, social interaction and restricted/ repetitive patterns of behavior. Autism may or may not be associated with language delays or intellectual disability.

Autism spectrum disorder (ASD) or *spectrum disorder*: A broad term used to describe a group of complex developmental brain disorders. ASD includes other

developmental disorders, such as PDD-NOS (Pervasive Developmental Disorder – Not Otherwise Specified), Asperger's Syndrome, Rett Syndrome, and Childhood Disintegrative Disorder (APA, 2013).

Autistic Diagnostic Observations Scale–2 (ADOS-2): The ADOS-2 is a standardized assessment. It is a semi-structured assessment used to diagnose ASD (Lord et al., 2012) and assess ASD across age, development and language. It is administered through observation and coding by a trained clinician.

Communication impairments: These refer to verbal, nonverbal, or partial verbal difficulties (Rees & Bellow, 2002).

Developmental Delays/Disorder (*DD*): Also known as Global Developmental Delay, and relates to children under 5 years old who fail to meet expected developmental milestones (APA, 2013).

Genetics: Genetics is the biological process of passing on genetic markers to offspring. For example, a person's appearance (height, hair color, skin color, and eye color) is determined by genetic traits (Feero, Zazove, & Stevens, 2011).

Intellectual Disability **(**ID**)**: The current, preferred term is *Intellectual Developmental Disorder*. This is a disorder having onset from birth onward that includes both intellectual and adaptive functioning deficit in conceptual, social and practical domains (APA, 2013).

Repetitive/restricted and stereotyped behaviors: A pattern of behavior that involves motor movements, and using objects or speech. There is a tendency for repetition, rigidity, facial expression, sameness, sensory arousal and/or routine that are

abnormal in intensity. These behaviors interfere with normal activity and could be seen as compulsive, stereotypic, a medical condition, or a result of a substance (APA, 2013).

Socialization impairments – These refer to difficulty in regulating emotional recognition, facial recognition, difficulty forming and maintaining positive relationships. They cause social ineptness and emotionally disengaged behavior (Radice-Neumann et al., 2007).

Spectrum Disorders - Any of a group of disorders each having symptoms that occur on a continuum and certain features that are shared along its spectrum, but manifest in markedly different forms and degrees (Mayo Clinic Staff, 2014).

Syndrome: A grouping of signs and symptoms that frequently co-occur and may suggest an underlying pathogenesis, course, familial pattern, or treatment selection (APA, 2013).

Assumptions

Every structure in the brain has specific physiological functions (Dukart & Bertolino, 2014). Therefore, when a region or structure of the brain is affected, it could adversely impact neurodevelopmental functioning, as exemplified by the three domains considered in this study. When functionality is compromised, collectively and simultaneously, it is assumed that it diminishes neurodevelopmental functioning, as measured by ASD severity. Severity on the spectrum is used to diagnose ASD. When considering severity and how it represents level of function, it is assumed that a given level might be represented by a point on the spectrum. Each point may be a specific disorder such as Asperger’s, Autism, or PDDc. For example, Asperger's is on the mild end of the spectrum, while autism is at a moderate point, and PDD is on the severe end.

Scope, Delimitations, and Limitations

A possible delimitation for this study was the use of archival data. Another delimitation y was administering the ADOS-2 instrument. The publishers of the ADOS-2 instrument require trained credentialed professionals to administer it. Because I was not trained to do so, I could not administer the ADOS-2. However, archival data adequately substituted for this purpose. Another delimitation of this study was the use of a special population. This study consisted of children and adults diagnosed with ASD. These individuals were a special population category. As such, the ability to administer assessments to this sensitive population was highly restricted. Using archival data resolved this issue.

A limitation of this study was the sample used. The sample pool had all been previously diagnosed with ASD and age and gender selected (non-randomly from the ADOS-2 pool). However, the data were randomly selected across all groups. There was no information on specific socio-economic backgrounds, such as culture, religion, ethnicity, sexual preference, or education. As the parameters of inclusion were broad, this study could be generalized to the ASD population.

Significance

The significance of this study was that I expanded the literature identifying the factors related to age and gender difference of ASD. Autism spectrum disorder is widespread and affects 1 in 55 individuals (ADDM, 2016). A wide array of neurological disorders is now placed under one entity, the ASD spectrum. According to the APA's (2013) *DSM-5*, there are currently no distinguishable diagnostic differences between individuals with PDD, autism, Asperger, genetic related autism disorders, childhood

disintegrative disorder, Rett syndrome, or Fragile X Syndrome. The ASD disorders were categorized by a severity measure that placed the ASD population on the spectrum with mild, moderate. or severe conditions.

More importantly, in this current study, I investigated age and gender differences in neurodevelopmental functioning of individuals with ASD. Statistical analyses were used to test the relationship between age, gender, the domain score, and total score. I used the ADOS-2 to help determine how age and gender differences were related to neuro-developmental functioning for individuals with ASD.

Social Change Implications

In this study, I found statistically significant age differences in the domain scores. This added to the body of knowledge on ASD and may contribute to the field by developing programs and new treatments for those with ASD. The social change proposed examined the relationship between age, gender, and ASD. ASD is a neurodevelopmental disorder that, atthis time, has not demonstrated a link between age and gender and the neurodevelopmental components of ASD. This research contains that information.

Chang (2014) reported that during brain growth and plasticity in childhood, children were more likely to respond to treatment resulting in a greater likelihood of recovery than during adolescence. Information on age and gender difference that provided data supporting Chang's study were found in this research. For example, Chang showed that there are differences in brain functioning and anatomy demonstrating that typically developing girls are more likely to grow out of stuttering more than boys. However, the current study examined a different angle of age and gender difference. It

may be interesting to explore further research together the implications of Chang's research and this current research.

Another social change implicated for the current study was advancing research in the ASD field. I found no gender differences among these indicators of functioning in individuals with ASD. It is hoped this information will spur further examination of this topic.

Summary and Transition

In summary, I explored whether differences in age and gender influenced functioning of individuals with ASD. Chapter 1 provided an overview of the study. The purpose of this current study was to examine how the differences in age and gender are related to total score and domain scores of communication, socialization and restricted/repetitive behaviors of ASD, as measured by the ADOS-2. Chapter 2 includes relevant research of the topic of age, gender, and the developmental basis of autism. Chapter 3 includes the outline of the research design and process of data collection for the research design. Chapter 4 detailed the statistical analysis of the data. Chapter 5 interpreted the findings and the implications of the study, and their significance vis-à-vis positive social change.

Chapter 2: Literature Review

Introduction

The purpose of this current study was to examine how differences in age and gender were related to total score and domain scores of communication, socialization and restricted/repetitive behaviors of ASD, as measured by the ADOS-2. The problem statement I identified for this study was that there is no known cause for 60-70% of those with ASD (Schaefer, 2016). I wrote the research questions to explore the correlation between age and gender, and the total and domain scores measured by the ADOS-2. The gap in the literature was the lack of research linking age and gender to neurodevelopmental components of ASD, as measured by the ADOS-2.

This study was quasi-experimental with non-randomized categorization of the participants, as described by Campbell and Stanley (2015). Archival data were used for analysis. There were two independent variables (age and gender) and four dependent variables (ASD domain scores and the ASD total score). The statistical analysis for this study included a MANOVA and a 2-way ANOVA to test for age and gender differences among the domain and total scores.

The problem that led to this study was that there is no known direct cause of ASD. The current literature showed that 30-40% of the etiology of autism was genetically related (Schaefer, 2016). There was no known common cause for the other 60-70% of the diagnosed population. In this study, I explored how age and gender differences were related to several neurodevelopmental components of ASD, as measured by the ADOS-2.

In this chapter, I highlight literature that supported and refuted various theories on a possible relationship between neurodevelopmental components and age and gender

across the autism spectrum. Autism spectrum disorder is a continuum consisting of several neuro-developmental disorders categorized by their severity and diagnosis. Many of these symptoms are sometimes masked, which may lead to misdiagnoses.

This chapter also contains various diagnoses associated with ASD and ASD-like symptoms. Although the onset of autism begins in childhood, there are many adults that are undiagnosed. As a result, an adult can be diagnosed later in life if ASD is not detected during childhood. It is common for those with ASD to not be tested for ASD at an earlier age due to various factors: resources, masked symptoms, parenting, etc. It is also common that females were tested for ASD at an earlier age due to stereotyping: boys tend to have masked symptoms (Daniels & Mandell, 2013). Daniel and Mandell also addressed inconsistencies in the research findings about the impact of age and gender on ASD. The current ASD spectrum, based on the *DSM-5*, was vague concerning ASD interventions such as referral, testing, diagnosis, and treatment (APA, 2013).

Literature Search Strategy

Databases and Other Sources

Library databases and search engines I used for this study were: *Academic Search Complete/Premier*, *PsychInfo*, *PsychArticles*, *Sage*, *Google Scholar*, *Google Search*, *ProQuest*, and *Expanded Academic ASAP*. I also used biology and psychology texts, medical references, professional organizational websites, the *DSM-IV-TR*, and the *DSM-5*.

Key Search Terms

Some of the key terms used to search for articles relating to this paper were: ADI-R, ADOS-2, age, Asperger, autism, autism spectrum disorder, autistic, brain injury,

executive function, genetic disorder, brain base behaviors, brain injury, brain insults, brain structure, childhood schizophrenia, communications symptoms, congenital brain injury, early infantile autism, gender, genetics, Kanner syndrome, motor function, neural systems, neural connectivity, neurodevelopmental disorder, neuropsychological assessments, pervasive developmental disorders, praxis, sensory function, stereotypic repetitive and repetitive behaviors, restricted/ repetitive behaviors, sensory/motor functioning, socialization symptoms, and traumatic brain injury.

Scope of Literature Review

The scope of literature searched ranges from the early 20th century (1908) to current research. The literature review includes literature on age and gender differences of ASD, the origin of ASD, and developmental stages based on age and gender. Finally, this section also includes a comparison fo development with ASD and typical development.

Age and gender differences in ASD. There were numerous studies conducted using the influence of age and gender on ASD. However, researchers reached inconsistent findings on the impact of age and gender difference on ASD (Daniel & Mandell, 2013). This gap in literature was the motivation for this study. There were no known research studies directly addressing aspects of neurodevelopment related to age and gender for those with ASD and measured by the ADOS-2. My objective in this study was to investigate if there was a relationship between age and gender and that of total score and domain scores as measured by the ADOS-2.

Daniel and Mandell (2013) researched age differences of those with ASD. They reviewed 42 peer-reviewed articles to assess the age at which ASD was diagnosed found

various results. Some researchers found that age related to cognitive impairments at the time that testing diagnosed individuals with intellectual disability (ID). Other researchers found an earlier age of testing to find ID to be a comorbid factor in ASD. An individual was initially tested and found not to fit into the ASD qualification, but later was retested and diagnosed with ASD. The authors of one found age and gender have no association with ASD diagnosis.

In contrast, other researchers found age differences at the time of diagnosis related to race, ethnicity, socio-economic status, educational setting, health setting, parental concerns, birth order, referral process, comorbidity, symptom severity, and geographic region had significant impacts on ASD (Daniels & Mandell, 2013). Discrepancies in studies were also found concerning the role of age with cognitive impairment. Some researchers found no association between age and cognitive impairments, while others found an inverse correlation. Yet others found a positive association. However, conflicting findings regarding race were more challenging to identify because some studies reported age differences to be related to race, while others found age differences connected to race related to a later diagnosis. Daniels and Mandell contended that further research was needed on age differences and their effect on ASD.

McGillivray and Evert (2014) conducted a study on gender and age of ASD. The researchers explored the effects of gender and age on stress and emotional distress in adults with ASD. The team attempted to address gender and age of ASD, but did not use the ADOS-2 instrument. They used several subscales (Depression, Anxiety and Stress) to differentiate the gender and age basis of ASD and compared the depression, anxiety and stress scales to determine age and gender differences. They found that there were

significant age and gender differences on these scales. ASD females were significantly depressed and anxious when compared to same-age males and younger females on the depression and anxiety scale. ASD females are more stressed than ASD males on stress scales. A finding of this study was that adult females with ASD were at higher risk for emotional vulnerability. However, this varies according to age and gender. McGillivray and Evert (2014) used self-reported scales to determine the statistical significance of their study.

Origin of ASD. Kanner introduced the diagnosis of early infantile autism in the 1940's (Edelson, 2006). However, Kanner did not assess children with autistic behaviors for cognitive or intelligence testing. In another early instance, Pollack (1958) reported that 30% to 40% of children with autism have mental retardation (Pilowsky, Yirmiya, Gross-Tsur, & Shalev, 2007). Similarly, Creak (1961) found that children with autism were more likely to have mental retardation claimed that these children were not educable because of serious retardation and childhood schizophrenia.

In the 1960s autism was known as early infantile autism (Gibson, 1968). Childhood schizophrenia was used to identity autism, as well as childhood psychosis (DeMyer et al., 1981). Autism and related terminologies began to appear more frequently in the 1970s. Childhood schizophrenia and psychosis were still used for most childhood mental health and developmental disorders. Lockyer and Rutter (1970) traced back hundreds of empirical and non-empirical claims that researchers were finding between 60%-90% of children with autism had mental retardation (Edelson, 2011). At the time, autism was classified primarily under mental retardation (Edelson, 2011). It was, and still is, easier to fund further research and subsequently diagnose mental retardation because

the topic of mental retardation has historically been more widely researched. Autism has been misdiagnosed and under-diagnosed because of a longstanding lack of diagnostic tools, lack of treatment and services, and lack of funding and insurance coverage.

In the 1980s, autism was still classified under early infantile autism syndrome and childhood schizophrenia (DeMyer et al., 1981). The *DSM-III* of the 1980s classified infantile autism under this developmental disorder. Unlike Kanner's criteria for autism diagnosis, the *DSM-III* differentiated between autism and mental retardation.

In the 1990s and 2000s, the topic of autism was becoming more prevalent in the research community and in public discourse because there was more emphasis on the subject. During this period, research on autism exploded. Experts were developing more diagnostic tools and programs for autism. The Asperger Syndrome was identified, which had also been misdiagnosed for many years. Research expanded into a search for the etiology of autism. There are numerous studies on the genetic basis of autism. However, there was no direct literature on the cause of the vast majority of autism.

Folstein and Rutter (2006) indicated that autism was associated with biological hazards that could lead to brain injury. Another controversial theory that was explored as a cause of autism was vaccination (Flaherty, 2011), specifically the childhood vaccine for measles, mumps and rubella (MMR). A widely publicized medical theory by Wakefield, a physician from Great Britain, in 1998. His research indicated that there was an autism phenotype activated by the MMR vaccine. This claim was later found to be based on fraudulent science. Recent debate on the topic of autism continues to occur because it is widely covered in peer-reviewed articles, popular writings, and the media. This led to great deal of misunderstanding and confusion on the topic of ASD. According to the

DSM-5, ASD is a lifelong neurodevelopmental disorder associated with deficits in social communication, social impairments, and repetitive/restricted patterns of behaviors (APA, 2013).

Age, Gender, and Neurodevelopment

The *DSM-5* states that neurodevelopmental disorders are a group of conditions with their onset during the early developmental period (APA, 2013). According to the *DSM-IV-TR*, some of the disorders in this category are mental retardation, autism spectrum, learning disability, pervasive developmental disorder, childhood developmental disorder, intellectual delays, etc. (APA, 2000). However, the *DSM-5* includes the following conditions as neurodevelopmental: intellectual disability, ADHD, specific learning disorder, genetic disorder, Fragile X Syndrome, tuberous sclerosis, Rett syndrome, epilepsy, and fetal alcohol exposure (APA, 2013). An individual diagnosed with autism is considered to be on the autistic spectrum because autism has a set of diagnostic criteria (Izuwah, 2012). Further, an individual could have autism as well as another neurodevelopmental disorder. If there is a display of severe cognitive and/or functional developmental symptoms, the *DSM-5* classification could be classified under developmental disorders.

Some neurodevelopmental disorders can often be recognized before 3 years of age (Izuwah, 2012), and most parents or guardians start recognizing developmental delays in their child. The child's development can be assessed through parental observation or routine pediatric checkups. If the child is not meeting expected milestones (e.g., delays in talking, walking, etc.), this could indicate that close monitoring of the child's development is needed. Other critical developments, such as intellectual progress,

are generally detected later in development. This is more prevalent with school-aged children because the deficiencies are seen in academic performance. Onset of these developmental disorders typically occurs before 3 years of age. However, autism and other developmental disorders might go undetected, undiagnosed or misdiagnosed for many years, or never. While there could be an onset of autism at or before 3 years of age, it may go undetected if not observed or properly assessed. Therefore, a person might be diagnosed much later in life.

Age and neural development. In normal brain development, the nervous system starts developing before birth and continues into childhood (Lenroot & Giedd, 2006). During the first neurodevelopmental stage, the neural circuit begins to form, starting with the neural tube of the embryo and nears completion after 3 to 4 weeks of gestation. This is the stage where birth defects, such as spina bifida, could occur. After 4-12 weeks the neural tube divides into two. One end of the neural tube differentiates into the forebrain and facial structures, and the other end becomes the spinal cord. The hollow center of the neural tube becomes the brain that eventually forms ventricles. The region around the ventricle (the proliferative zone) produces young neurons. By 12-20 weeks, the young neurons multiply rapidly and migrate to the cortex. From 24 weeks to 4 months after birth, rapid neuron deaths occur, and their number is reduced by half.

During the second neurodevelopmental stage, myelination of the brain stems begins by the 29th week (Lenroot & Giedd, 2006). Myelination occurs in the brain stem from the interior cortex to the superior cortex, then from the posterior cortex to anterior cortex. Maturing myelination sheaths become thinner and more vulnerable to environmental and age factors. Myelination continues near the temporal lobe throughout

the second and third decade of life. The neuron's cell bodies become the gray matter, and the myelination axon becomes the white matter of the brain. The white matter increases with age and starts decreasing around the fourth decade of life (Lenroot & Giedd, 2006).

The third neurodevelopment stage is the proliferation and organization of synapses, which begins around the 20th week (Lenroot & Giedd, 2006). Synaptic density increases rapidly after birth and continues to increase. By 2 years of age it is 50% more than what is seen in adults. The synaptic density peaks at the visual cortex by four months post-natal, and then at the prefrontal cortex at 4 years of age. This is followed by a regional loss of synaptic connections. By 15 weeks, the surface of the brains also folds into sulci and gyri. The major sulci, except for the occipital lobe, are in place by 28 weeks of gestation. Almost all the gyri are in place by birth, and the elaboration of secondary and tertiary continues to increase in complexity after birth (Lenroot & Giedd, 2006).

The growth of the nervous system is rapid until 2 years of age, when 80% of the adult brain weight is achieved; at 5 years of age the brain has reached 90% of adult weight (Lenroot & Giedd, 2006). The remodeling of the gray and white matter of the brain continues until the third decade. Total cerebral volume peaks for males at 14.5 years and for females at 11.5 years. Males have 9% more brain volume due to body mass index, and this is not an indicator of performance differences. There are some specific functional and structural differences: males perform better with spatial ability due to a larger hippocampus. Brain structure differences vary due to gender, genetics and environmental factors. Stress during development may result in compensatory

physiological responses that could affect brain structures and functions (Lenroot & Giedd, 2006).

During typical brain development, there is a sensitive period, or window of opportunity, that occurs (Johnson, 2005). This is the optimum period for the most effective brain and behavior development. The sensitive period is related to the sensory domains during postnatal brain development. During the first decade, neuro-anatomical development of the brain changes in level of motor, perceptual and cognitive abilities. When the sensitive period is closed (self-terminated), the development of achieving full function may be limited for specific sensory behaviors (Johnson, 2005). Plasticity could be terminated during this critical period, and there are sensitive periods for specific processes. The consequence is specific to the learning process for each area. There are also multiple and various sensitive periods during development (e.g., there are critical periods for vision, acuity, face processing, language, etc.). A sensitive period for one area may not correspond to another during a specific time or during later functioning or interregional connection. Thus, specific brain damage could lead to deficits in face processing but could have less impact on language acquisition abilities (Johnson, 2005).

Sensitive periods have fixed time windows (window of opportunity), during which specific regions are sensitive to their interconnections with other regions of the brain (Johnson, 2005). Johnson reported differential neuroanatomical development of brain regions is used to determine an age when a particular region is likely to become functional. From a behavioral viewpoint, maturation of particular regions of the brain moves from regions of the cerebral cortex, to newly emerging sensory, motor, and

cognitive functions. Any new behavioral task at a particular age is attributed to maturation of new brain area.

In post-natal brains, the development of the cerebral cortex may involve a process of organizing patterns of interregional interactions (Johnson, 2005). During development, activity-dependent interactions between regions sharpen the functions of those regions such that the activity becomes restricted or specific to a narrower set of circumstances. New behavioral competencies during infancy may therefore be associated with changes in activity over several regions. The functional brain develops skills and learns in ways that involve changes in neural activity. The changes seen during functional brain development in infants and children as they acquire new perceptual or motor skills were similar to changes seen in adults' complex perceptual and motor skills acquisition (Johnson, 2005).

In order to understand disorders or impediments affecting the brain, it is important to understand the origins and mechanics of neural development in healthy and abnormal brain networks. Changes in normal behavior and at-risk behaviors are related to radical developmental changes in structure and function of the brain (Vertes & Bullmore, 2015). Synaptic connectivity, axonal myelination, cortical thickness, and white matter volume are all markers for normal or abnormal development (Vertes & Bullmore, 2015).

Synaptic density peaks at 1 year of age and is followed by extensive reduction in childhood (Johnson, 2005). Major modules/hubs of neural structural connection are stable at birth if normal, but neural connections (network interactions) continue to increase via long fiber pathways that keep linking until adulthood (Johnson, 2005). For example, cognitive processes originate from network interactions between neurons over long and

short distances, which result in behavioral changes if the network is compromised. Despite continuous changes in the integrative neural networks over time, module/hubs of the neural network are fixed by the age of two (Johnson, 2005). Primary sensory and motor systems are functionally delineated at birth, but longer functional connections are limited under age two. Functional networks are reorganized during development, with anterior cingulate and prefrontal nodes splitting from other frontal nodes and tightly connecting with insular and thalamic nodes (Johnson, 2005).

Gender. According to Kimura (2002), men and women differ in intellectual abilities, gender specific behaviors, and problem solving. This is due to sex hormone interactions early in life and is related to environmental and social demands. Sex hormones are regulated by the hypothalamus in the base of the brain. Men possess the Y-chromosome, which regulates testosterone and for females, the hormone is estrogen (Kimura, 2002).

Gender-specific behaviors regulated by sex hormones influence why males are more aggressive and females are more nurturing. In regard to intellectual functioning, men differ from women in patterns of ability, not intelligence. Such patterns of ability for men are performing better in spatial tasks, mathematics, navigation, and target motor skills. Women are better in word recall, precision, verbal memory, and matching items (Kimura, 2002). Sex differences in problem solving can be demonstrated in children as young as three and four. However, manipulation of hormones during the critical period can alter gender-specific behaviors. The right and left hemispheres of the brain are asymmetrically organized by speech and spatial functions in males (Kimura, 2002). On the other hand, part of the corpus callosum is apparently larger in women, which gives

them better communication between hemispheres and is why damage to one hemisphere in women has smaller effects. The amygdala volume increases with age in males, as does the hippocampus in females, showing gender specific maturation (Lenroot & Giedd, 2006).

ASD Development versus typical development: Age and gender effects. According to Pangelinan et al. (2011), cognitive and motor functions are inter-related based on development of brain (cortical and subcortical) structures. Cognitive and motor skills are related to behavior and brain structure. Considering the trajectory of cortical and subcortical brain development, children with developmental disorders exhibit impaired motor functions. Those with ASD and/or ADHD show structural abnormalities in brain regions that mediate cognitive and motor circuits.

Giedd and Rapoport (2010) conducted their research on neural development using MRI scans, and reported that white and grey matter volume growth takes place in an inverted U shape, which peaks at age 14.5 for boys and 10.5 for girls. The brain size is at 95% of its peak by the age of six. Between 5 to 11 years old, the frontal and occipital volume increases in size. From ages 7 to 11 years old, the cerebellum reaches adult volumes in females. The cerebellum is linked to motor control, emotional processing, and higher cognitive functions. Cerebellar development in its characteristic shape peaks at 11.3 years for girls and 15.6 for boys. In contrast, cerebellar hemispheric lobes do not change with age (Giedd & Rapport, 2010).

White matter, that is myelin wrapped around the axon, increases the speed of neural signaling (Giedd & Rapport, 2010). Myelin also modulates time and synchrony of firing and signaling patterns. For children and adolescents, the white matter volume

increases with greater connectivity and integrated neural circuitry (Giedd & Rapport, 2010). Similarly, grey matter volume growth follows the inverted U shape. Cortical grey matter changes in density between4 to 20 years old. The earliest changes start in primary sensorimotor areas, and the last in higher order areas such as the dorsolateral prefrontal cortex, inferior parental, and superior temporal gyrus (Giedd & Rapport, 2010). Females' grey matter volumes are reached 1-3 years earlier due to timing of gene expression and age. In addition, the developing physical body indicates changes between the early maturing limbic system and later maturing frontal systems. For example, the limbic and frontal dynamic, and cognitive system is critical for decision making during adolescence. Collectively, the decision making system for adolescents is regulated by high arousal, peer pressure, and consequences, together known as hot cognition. Giedd and Rapport (2010) reported that the mechanisms and influences on structural and functional brain development in childhood and adolescence help harness the brain's developmental plasticity for development.

Hassan, Walimuni, and Frye (2012) showed that early developmental events have an impact on gray matter, limbic structures, and hippocampus volume. This indicates a neuro-biological disease basis for ASD. Children with ASD show hippocampus size increasing with age. The pattern of hippocampal volume in ASD children suggests a disturbance in early brain development. Also, ASD children have larger limbic structures (Hassan et al., 2012). The brain and regional volume of cerebrospinal fluid in healthy controls is less than 10%, compared to a cerebrospinal fluid fraction of 40% in ~~healthy and~~ autistic brains. Increased hippocampus volume in autistic patients ages seven to eighteen is due to age-driven degeneration. Increase in hippocampus volume in children

with ASD can mark an embryonic or early post-natal stage due to the accumulation of pioneer (cortical) neurons (Hassan et al., 2012). In normal development, pioneer neurons are eventually trimmed, and it appears that autism spectrum disorder can be related to the growth of these neurons. For instance, Asperger children ages nine and above had increased white matter volume, which indicates a loss of microstructures and impaired axons (Hassan et al., 2012).

According to Cheng, Chou, Fan, and Lin (2011), ASD is characterized by aberrant neurodevelopment as the ASD brain undergoes precocious growth followed by decelerated growth during the early post-natal period. A failure cascade is shown for typical ASD brain development. For example, head circumference could be normal or below size at birth (Cheng et al., 2011). This is followed by an increase growth to the 84th percentile in the first year. Between the ages of two and four, there is a 90% decline in growth rate in 5-10% of these abnormally enlarged brains. Thirty seven percent (of this 5-10 %) demonstrate macrocephaly and the brain shifts to abnormally slow growth (Cheng et al., 2011). The severity of ASD can be determined in infancy by brain growth that demonstrates neuroanatomical abnormalities. It is not common for adolescents to be affected by rapid brain growth, but a delay during infancy may have not occurred. If adolescent rapid brain growth occurs, it is considered to be within the mild end of the ASD spectrum, such as high functioning autism or Asperger's (Cheng et al., 2011).

White matter enlargement occurs 18 months and 4 years and surpasses that of grey matter growth (Cheng et al., 2011). There is a 6-12% enlargement for grey matter through adolescence and adulthood. Grey matter is localized within the frontal-striatal and parietal networks, and some may occur in the dorsolateral prefrontal and medial

frontal cortex (Cheng et al., 2011). High functioning ASD children have less grey matter volume increase in the bilateral caudate and left thalamus. They also show cortical thickness and an increase in the parietal and temporal cortex. ASD adults show a decrease in the inferior frontal gyrus, inferior parietal lobule, and superior temporal sulcus (Cheng et al., 2011).

Such cortical thinning in the inferior frontal gyrus is related to impaired social skills and communication (Cheng et al., 2011). Cortical abnormalities generally are connected with age and severity of social skills deficits. Abnormal structure and function of adolescents' brains often evidence more desaturation in the right inferior parietal lobe. For adolescents with ASD and having abnormal regional grey matter volumes, enlargements in the medial prefrontal gyrus, cerebellum, and superior parietal lobule appear more consistently (Cheng et al., 2011). These individuals also have larger volumes in medial prefrontal cortex, but smaller volume in the lingual cortex. This explains the social effect of high functioning ASD adolescents. Typical adolescence cortical volume increases in preadolescence (12 years), followed by a post-adolescent (young adulthood) decrease (Cheng et al., 2011). However, ASD adolescents' grey matter volume on the right inferior parietal reaches adult size by age 14.

Theoretical Foundation

The theoretical framework for this neurodevelopmental study was the work done by Zielinski et al. (2012), and pertains to the neurobiological basis of behaviors in autism. Zielinski et al. (2010) based their study on the relationship between biological structures and functions of the neural network, and the behaviors that result when there is a disruption. Researchers pinpointed abnormalities that lie within the brain's neural

network in autism and effect behaviors. Zielinski et al. focused on the ICN, or resting state, of the canonical domain. The ICN includes SN and DMN components, where disruptions are found. These areas are responsible for socio-emotional and communication skills. Deficits in these areas characterize autism. Zielinski et al. investigated how these symptoms of autism are linked to SN and DMN biological components.

Neurobiology draws from the anatomy and physiology of the brain and considers how changes in the brain influence specific behaviors (Morris, Lazo, & Smith, 2004). The biological basis of autistic behavior impacts the many actions associated with communication, socialization and repetitive/restricted stereotypical behaviors. The neurological components of communication provide the ability to interpret an action and respond to it (Swettenham et al., 2012). Therefore, the physiology and anatomy involved in communication behaviors have to be aligned with each other to function normally. According to Zielinski et al. (2012), the part of the brain involved with communication is the DMN region of the ICN architecture. Zielinski et al. found that altered connectivity in the DMN region of ASD impairs communicative behaviors.

Neurodevelopmental components of socializing behaviors can be disrupted within the SN system. The SN is comprised of various structures in the brain: the frontoinsular (FI) and dorsal anterior cingulate, as well as subcortical structures that include the amygdala, substantia nigra, and ventral tegmental area. These structures are responsible for conflict monitoring, autonomic responses, and reward processing. It also integrates external stimuli to internal states to maintain homeostasis in regulating related behaviors. The FI is the hub of the SN (Zielinski et al., 2012). The FI is hypoactive in autism and

undergoes early degeneration, which creates social-emotional dysfunction. Within the SN, interconnections between its critical nodes may be malformed and the network architecture may not mature, thereby leading to deficits in socio-emotional behaviors and cognitive processing. The impact on cognitive and behavioral processing leads to a breakdown in appropriate social guidance, lack of processing social and emotional cues, and abnormal engagement in cognitive processing (Zielinski et al., 2012).

There are also neurologic components of repetitive, restrictive, stereotypical, or motor function behaviors of ASD (Muehlmann & Lewis, 2012). These researchers focused on the restricted and stereotypical behaviors associated with autism and reported evidence of alterations in the development and expression of stereotypical behaviors in the cortical basal ganglia. Lewis, Gluck, Beauchamp, Keresztury, and Mailman (1990) conducted a study of non-primates that were socially deprived early in life. They found an association between stereotypical behaviors and alterations in cortical basal ganglia functions. The brain-behavior relationship was also associated with dopamine receptor sensitivity (Lewis et al., 1990).

Lewis and Kim (2009) noted that mediation of repetitive behaviors lies in the neural pathways. Neural connections arise from the cortex to the striatum, lead to the basal ganglia nuclei, then continue to the thalamus and circle back to the cortex. This is an intricate connection, considered a five-loop circuit, and regulates motor and oculomotor functions through the dorsolateral prefrontal, lateral orbitofrontal, and anteriorcortical cortexes (Alexander et al., 1986; Langen et al., 2012). The five-loop circuit is responsible for motor, cognitive and affective functions. Study on ASD has found that the motor circuit mediates repetitive motor movements. There are two distinct

pathways from the striatum, identified as the caudate or putamen. The two pathways are known as the direct and indirect pathways. The direct pathway facilitates movements and the indirect pathway inhibits them (Gerfen et al., 1990). Any irregularities in the pathways will affect movement, which is a factor in repetitive behaviors. Neuroimaging findings show a volumetric relationship with repetitive behaviors in autism, and was demonstrated by a decrease in white matter (Muehlmann & Lewis, 2012).

Swettenham et al. (2012) examinedthe biological basis of behaviors on the three dimensions of neurodevelopmental components. Their focus was on the perception of pointing gestures in children, which involves the integration of social, communication, and motor functioning behaviors. The team reported a lack of pointing gestures, a lack of interpreting pointing gestures, and the inability to follow other's pointing gestures. These skills are delayed in ASD, and limit the opportunity for social, communication and motor functioning behaviors (Camaioni, Perucchini, Muratori, Parrini, & Cesari, 2003). Pointing is restricted due to a lack of coordination in muscular-motor function. The biological motion of pointing involves eye gaze movement and configuration of the arm and hand. Therefore, the perception of pointing (or lack thereof in ASD) involves integration of social, communication and motor-functioning behaviors. The results of this study therefore reinforced the biological basis of behaviors presented in ASD.

Neurodevelopmental Components

ASD domains. This section addresses neurodevelopmental components in abnormal and normal development. As already noted, the three domains affected by ASD are social interaction, communication and restricted/repetitive behaviors. The typical

development of the neural system will be discussed, as well as ASD and other impediments to neurodevelopment.

***Social interaction*.** Radice-Neumann et al. (2007) noted that the most common areas of the brain that are likely to be damaged during brain injury involve emotional controls. The three areas of the brain commonly associated with emotional controls are the prefrontal cortex, limbic system (amygdala and temporal lobes), and parietal cortex. These areas are all connected or interlinked to socio-emotions. The parietal lobe and limbic system are responsible for noticing and analyzing facial features that demonstrate emotions. The prefrontal cortices are necessary for experiencing emotions and associating events with emotional experiences (Radice-Neumann et al., 2007).

Part of the prefrontal cortex, the ventral medial portion, associates events with an emotional experience, such as developing and storing emotional events (Radice-Neumann et al., 2007). Individuals with damage to this area of the brain have difficulties recognizing bodily affect. The damage to the ventral medial may result in poor social behavior. This is reflected in absent or reduced feelings of emotions, which may affect the ability to recognize the emotions of others. The limbic system (temporal gyrus and amygdala) processes facial features (Radice-Neumann et al., 2007). The amygdala is responsible for processing emotional responses such as fear or dangerous situations. An example is the 'fight or flight' response. People with amygdala damage have difficulty identifying facial expressions in whole or in part. They tend to avoid the eyes, the area around the eyes, or eye contact completely, all of which limits their facial recognition abilities and creates difficulty interpreting others' emotional state (Radice-Neumann et al., 2007). In cases of parietal lobes damage, individuals have difficulty discriminating

tactile sensory information. This affects one's ability to sense changes in the body, which minimizes sensing emotional changes. In turn, this may affect the individual's response to emotional stimuli and their interpretation of another person's emotions (Radice-Neumann et al., 2007).

Any impact or disruption to the prefrontal cortex, limbic system, and parietal lobes could affect the ability to recognize and process emotional information (Radice-Neumann et al., 2007). The structures and functions within these regions are necessary collectively for social-emotional performance. After injury to the emotional area of the brain, increased social problems may appear. Some of the social problems include an inability to interpret gestures, social inappropriateness, and an indifference similar to ASD (Radice-Neumann et al., 2007).

Communication. The anatomy of communication is the same for both sexes, but there are some sex differences in structure size and function (Nikolaenko, 2005). Sex differences and brain organization related to verbal function tasks were found both in adults and children between 5-15 years old. Sex differences in the human brain are more marked when looking at the differences of verbal skill for women, and spatial abilities for men (Coscove, Mazure, & Staley, 2007). There are sex differences in brain organization for specific language tasks. The sex difference in linguistic processing is demonstrated by accuracy performance reflected in specific brain regions (Burnman, Bitan, & Booth, 2008).

Sex differences in brain volume in gray and white matter is specific to gender (Coscove et al., 2007). The anatomy of the language system involves the anterior (Broca) and posterior (Wernicke) hemisphere temporal lobes. In women, the gray matter volume

in the frontal lobe and Broca's area (anterior hemisphere) are involved in language. In men, this is reflected in the gray matter volume of the frontal and parietal lobes.

Sex differences in children show that verbal capabilities are higher in girls than boys (Nikolaenko, 2005). This could be due to the auditory-verbal connection within the left hemisphere in girls. In boys, the neural connections are more inter-hemispheric. This demonstrates more interconnective interferences for boys. For example, a reading impairment or semantic paralexia, is seen more in boys than girls.

Sex differences for speech show that impairments in speech (aphasia) occur more when the anterior hemisphere is impacted (Kimura, 2002). Similarly, aphasia is higher in men with posterior hemispheric damage. Aphasia is the inability to produce and understand speech. Kimura indicated that women with posterior brain damage are less likely to experience apraxia when compared to men. Burnman et al. (2008) also indicated that language tasks activate different brain areas for boys and girls.

Restricted/repetitive behaviors. One of the primary characteristics of ASD is repetitive/restricted and stereotypical behaviors. According to South, Ozonoff, and McMahon (2007), these behaviors are related to cognitive rigidity and weak central coherence. Variability of repetitive/restricted and stereotypical behaviors across the spectrum depends on phenomenology and co-morbidity (Muehlmann & Lewis, 2012). Phenotypic and co-morbidity variations are due to overlapping pathophysiology, which suggests neural circuitry involvement (Bodfish, Symons, Parker, & Lewis, 2000). Repetitive/restricted and stereotypical behaviors are based on the neurobiology of these behaviors.

Muehlmann and Lewis (2012) focused on the environmental causes and

neurobiology of restricted/ repetitive stereotypical behaviors and elaborated on the environmental conditions that induce such behaviors. They noted that environmental deprivation leads to repetitive behaviors in non-human primates. The neural pathway that is activated in repetitive behavior is the cortico-striato-thalamo-cortical circuitry (Muehlmann & Lewis, 2012). This circuit relays from the cortex to the striatum, on to the basal ganglia nuclei, then to the thalamus, and back to the cortex. This circuit is comprised of multiple parallels loops that have distinct structures and functions. This circuit mediates sensorimotor, cognitive, and affective functions. When this circuit is compromised either structurally or functionally, maladaptive behaviors are demonstrated such as the restricted/repetitive or stereotypical behaviors of autism (Muehlmann & Lewis, 2012)

Nobile et al. (2011) pointed out the neurodevelopmental components of repetitive/restricted behaviors. They indicated that body/motor movements are a notable marker in a child's first year, before social or communication difficulties may become apparent (Esposito & Venuti, 2008; Teitelbaum et al., 1998). The researcher found that motor movements are an essential criterion for diagnosing ASD. They also examined arm movements used for balancing when walking. The part of the brain responsible for maintaining balance is the cerebellum. Injury to this area may result in abnormalities and immaturity and underdevelopment of the neural system for motor coordination. Abnormal movements are noticeable from early stages due to abnormal gait sequencing, delayed development of walking, lack of falling response reflex. Nobile et al. attributed the abnormalities to be a result of an immature neural system.

Nobile et al. (2011) conducted an explanatory quantitative research to explore

motor dysfunction in ASD children, ages six-fourteen. Sixteen ASD children and 16 healthy controls participated in their study. The independent variables were gait parameters and dependent variables were the scores on the ADI-R test (Rutter, LeCouteur, & Lord, 2003; see Table 1). The researchrs used factorial analysis of covariance (ANCOVA) to compare gait parameters between the ASD and healthy control groups. The FSIQ (full scale IQ) was used as the covariate in all between-group comparisons.

Nobile et al. (2011) used a quantitative analysis of children with autism and healthy controls. The procedure used an evaluation of linear gait parameters, spatio-temporal and kinematic parameters, upper body kinematic parameters, and walk orientation/smoothness using an automatic motion analyzer. Children with ASD demonstrated less fluidity in walking, a stiffer gait, trunk postural abnormalities, difficult maintaining a straight line, and an increase of jerk type behaviors in comparison with healthy controls. Based on the data from the study, the researchers found a complex motor dysfunction that involves cortical and subcortical areas of the brain. If there is brain damage or deficit in the neural system, the integration of sensory-motor information within this motor network may affect the connections of the frontal-cerebellum-thalamus network (Nobile et al., 2011).

The researchers stated that injury to the specific part of the brain responsible for motor/sensory functions could manifest as the motor impairments exhibited in ASD. The authors noted that difficulties observed in motor functioning could be contributed by generalized praxis deficit, which could account for the impairments of basic motor skills in ASD. Praxis reflects abnormalities in neural circuits of the brain that are responsible

for building internal representation of body schema and acquisition of sensory movement or motor sequence programming needed to execute them. Nobile et al. (2011)also used the scores on the ADI-R (socialization, communication, sensory/motor function) as the dependent variable to confirm sensory/motor function as a domain of ASD. They also used the scores on the ADI-R to compare ASD and ABI in order to examine the relationship between them.

ASD and Neurodevelopmental Disorders

According to the *DSM-5* classification, autism or autism disorder is a neurological developmental disorder that affects three domains: social, communication, and restricted/repetitive behaviors (APA, 2013). Autism is specific to these domains. However, there may be comorbid language delays and/or intellectual disability. On the other hand, autism spectrum disorder is a broad category of several disorders or multiple facets of a disorder (Autism Spectrum Disorder Fact Sheet, n.d.). Symptoms of ASD differ from each other and affected individuals differ among each other. The severity of symptoms differs between individuals as well. It is called a spectrum because the symptoms and severity can vary greatly between individuals on the spectrum. Just as no two people with ASD look alike, so no two ASD individuals would present with identical autistic symptoms. There is almost always a variation of symptoms for individuals with ASD. The ASD umbrella includes autism, Pervasive Developmental Disorder, Rett syndrome, childhood disintegrative disorder, and Asperger's syndrome. Therefore, if someone that has autism, that individual falls along the ASD spectrum. However, not everyone on the ASD spectrum has autism. For example, someone with PDD is on the autism spectrum disorder and not autistic.

Autism Spectrum

According to the *DSM-IV-TR,* the five most common disorders under the ASD umbrella were: Autistic disorder, Asperger's disorder, Pervasive Developmental Disorder, Rett Syndrome and Fragile X Syndrome (APA, 2000). *DSM-5* does not differentiate between these disorders; most of them are now considered ASD (APA, 2013). There are many possible causes of ASD, include genetic disorders, hereditary conditions, brain injury, developmental disorders, and environmental insults.

Genetic disorders. Among the many types of genetic disorders, Rett is considered part of the ASD. Rett is the only disorder identified with a genetic mutation related to the MECP2 gene (Hsiao-Tuan et al., 2010) and is a neurodevelopmental disease affecting 1:8500 females (Derecki, Privman, & Kipnis, 2010). Rett is found mostly in females due to mutations in the X chromosome. Far more rarely, cases of Rett occur in males (Young et al., 2008). Rett was previously diagnosed under infantile autism. Both Rett and infantile autism have similar symptoms, including disruptions in language and social interactions, as well as repetitive behavior. Females are more likely to be diagnosed with autism earlier in life. In many cases, the diagnosis may later change to Rett syndrome. Individuals with Rett may have small brains, but there is no known indication of initial atrophy. The Rett child has normal head circumference development until 5 months old. At that point, the rate of head growth begins slowing (Derecki et al., 2010).

Some genetic disorders may fall under the autistic spectrum while others may only mimic autistic symptoms. Common genetic disorders include Fragile X Syndrome, Rett syndrome, hypotonia (Gong, Sun, Jiang, & Gong, 2011), Angelman syndrome,

Cornelia de Lange syndrome, Prader-Willi syndrome, Smith-Magenis syndrome (Oliver, Berg, Moss, Arron, & Burbidge, 2011), phenylketonuria (PKU), tuberous sclerosis complex, Down syndrome, Tourette syndrome, and Cowden syndrome (Bauer & Msall, 2011). However, there are many other genetic disorders associated with ASD.

Fragile X Syndrome, which had been classified in the autistic spectrum (Gong et al., 2011), is a brain developmental disorder with symptoms ranging from social disturbances and social anxiety, to autism (Brodkin, 2008). Fragile X is no longer part of the ASD in *DSM-5* (APA, 2013). Fragile X Syndrome is due to genetic mutations and environmental factors occurring during brain development. Such genetic mutations could cause hypermylenation of brain cells resulting in developmental disorders.

Hypermylenation is a misregulation of myelin, which is the tail portion of neurons within brain cells (see Figure 3). Hypermylenation may result in misregulation of synaptic development cause abnormal myelin function. Myelin (see Figure 2) is an insulating sheath (protein) around neuronal axons (Pearson, 1995-2002). This type of hypermylenation could be a result of genetic mutation, which sometimes manifests as mental retardation. Men with the Fragile X genetic component are 100% likely to be affected by mental retardation, while 50% of females with the same component are likely to be so. Ninety percent of males affected with Fragile X may exhibit symptoms of autism, which can include atypical social interaction, lack of eye contact with others, social anxiety and avoidance, perseverative speech, stereotypical behavior (e.g., hand flapping, repetitive behaviors), hypersensitivity to sensory stimuli, impulsive aggression, or self-injurious hand biting.

Hereditary conditions. Like Fragile X, Rett syndrome is a hereditary condition (Hsiao-Tuan et al., 2010). Both Fragile X and Rett are closely linked to autism. Studies indicated that siblings of those with autism have also been diagnosed with the disorder. This includes twins, monozygotic and dizygotic, who are likely to be affected.

Environmental factors. Environmental insults include carcinogens, teratogens, infectious agents, parental transmission or contamination, prenatal infections, other substances, and congenital brain infection (American Cancer Society, 2014). Carcinogenic contaminations can be carried genetically by parents (biological) or by external exposure (environmental factors). Some common environmental factors such as carcinogens include the following: lifestyle factors such as nutrition, tobacco use, substances, alcohol, and lack of physical activity; naturally occurring exposure such as ultraviolet light, radon gas, and infectious agents; medical treatments such as chemotherapy, radiation, and immuno-suppressant drugs; workplace hazardous exposures, household hazardous exposures, and pollution (American Cancer Society, 2014). Various national and international agencies classify carcinogens (see Appendix A).

Brain impact. According to the Brain Injury Association of America (2015), brain injury is a result of any form of insult, blow or impact to the brain that resulted in impairment of cognitive, behavioral, and/or physical functioning. Brain injury, or brain damage from either internal or external sources, can lead to different types of disorders (Middletown, 2005). There are several types of brain damage, which can occur during birth or after birth. The different types of brain injuries are acquired (ABI), traumatic (TBI), congenital (CBI) and degenerative (DBI).

Acquired brain injury. Typically, ABI occurs at a cellular level or by an internal cause before or after birth and is not degenerative. Acquired brain injury includes traumatic and congenital brain injuries, which can take place any time after conception (Middletown, 2005). Examples of acquired brain injury include, but are not limited to, trauma, systemic illness, metabolic disturbances, central nervous system tumors, infections, and toxins which may result in head injury, phenylketonuria, birth delivery, drugs and alcohol, seizures, tumors, brain malformations, diabetes, sickle cell anemia, meningitis, encephalitis, etc. These injuries could lead to some degree of impairments such as physical, social, cognitive or educational.

Traumatic brain injury. TBI is any injury to the brain after birth and is an acquired brain injury (Ciuffreda & Kapoor, 2012). It could be caused by a sudden onset that is non-progressive and exclusive to birth trauma. This can be due to an external force, the result of a trauma, such as a blow to the head. It is not a degenerative disease. According to Ganesalingam, Yeats, Taylor, Waltz, and Stancin (2011), children impacted by traumatic brain injury between the ages of two and seven, suffer from various deficits, including the ASD criteria, which are deficits in language, social incompetency, inhibitory control, and motor skills. These deficits can mimic ASD-like symptoms.

Congenital brain injury. CBI can result from an injury to the brain due to infections, genetics, or birth trauma. Infections during pregnancy can enter the fetal brain causing permanent brain dysfunctions, especially so because the brain is developing (Bonthius & Perlman, 2007). Children with congenital infections can sustain neurological deficits such as microencephaly, enceohalomalacia, choroioretinitis, porencphalic cysts, neuronal migration disturbances, periventricular infection, and cerebellar hypoplasia.

Cerebellar hypoplasia (missing or small cerebellum) can also be caused by genetic mutations. Genetics can play a similar role resulting in mutations affecting the brain during pregnancy and after birth. Developing abnormalities can be evident at birth or remain hidden. If occult, these could become more evident in later months or years (Bonthius & Perlman, 2007). One example of a genetic disorder is Rett, which is not apparent at birth. This is due to the fact that at birth, the Rett's brain develops normally, but starts decelerating a few months later (Derecki et al., 2010).

Degenerative disorder. Degeneration is a disorder of the brain due to a neurological disorder (Davidson et al., 2008). This can be associated with age, as is most often the case with Alzheimer's disease. An example of a childhood degenerative disease is spina bifidia, which can begin during the third or fourth week of embryotic development if the spine's neural tube does not close, and lead to the possibility of a neural tube defect (Davidson et al., 2008). Spina bifidia is a neurological disorder that can be induced by genetics or environment. Surviving embryos may suffer from some type of congenital malformations. In the United States, 1-2 cases in 1000 are seen.

Rationale for Choice of Theory

The theory for this study was that neurodevelopmental features affect the functioning of individuals with ASD. Disruption of the brain was hypothesized to impact behaviors. The rationale for this choice of theory is supported by Zielinski et al. (2012), who reported that disruptions of specific regions of the brain are consistent with the impairments found in ASD behaviors. As such, if there were brain abnormalities in a specific region of ICN system, the outcome will be displayed by behaviors seen as ASD symptoms.

The brain has specific areas that are responsible for different functions (Zielinski et al., 2012). The neurons (i.e., brain cells, see Figure 1) that reside in these areas are the messengers and storehouses for specific information. The types of information processed and relayed through these neurons are for memory, cognition, vision, optical, auditory, touching, emotions, violence, intelligence, motor movements, sensory movements, learning, performance, behaviors, language, all activities, all thoughts, etc. Therefore, neurons may control, process and conduct all human activity, whether voluntary or involuntary.

Disruptions such as injury, deficits, abnormalities, diseases, genetics, infection, surgery, seizures, or environmental insults to neurons may lead to impairments in processing accuracy and conduction of information (Zielinski et al., 2012). Any of these disruptions may consequently lead to some deficiencies in the neural network. Injury in the ICN network responsible for socialization, communication and repetitive could indicate autistic symptoms. This could justify why injury to the areas of the brain responsible for communication and socialization, and repetitive/restricted neural system could mimic autism. Zielinski et al. (2012) identified the ICN region of the neural network as consisting of the SN and DMN structures. The SN is responsible for socialization, while the DMN controls communication (Zielinski et al., 2012).

Scanning specific regions of the brain shows regionally selective abnormalities and demonstrates differential brain structures. However, proximate regions of the network model of autism shows that areas outside the network region may not be necessarily affected (Zielinski et al., 2012) and suggests ASD is regionally based. Functional and structural abnormalities in the ICN-specific regions indicate network-

level abnormalities characteristic of autistic neurobiology. The brain structure showing mal-development in the neural interconnectedness network architecture will result in domain-specific abnormalities characteristic of autism. Functional connectivity MRI scanning (fcMRI) shows specific regional activity during the normal resting state without direct stimulation in ASD. On the other hand, fcMRI shows deactivation during cognitively-demanding stimuli in ASD, which points to functional abnormalities. The researchers commented that there seems to be a relationship between the abnormalities found within regions of the neural network and autism (Zielinski et al., 2012).

The fcMRI showed abnormalities in ASD brain structures and functions compared to controls (Zielinski et al., 2012). The neural abnormalities can lead to decreased oxygen-blood flow, decreased or increased grey matter, decreased and increased white matter, increased and decreased interconnectedness of neurons, and underdeveloped regions (Zielinski et al., 2012). These were also some impairments that compromised the ICN system specific to ASD.

Neural level disruptions occur within both grey and white matter (see Figure 8). Grey matter consists of neurons composed of cell bodies, axon terminals, and synapses. White matter is made up of axons (nerve fibers). The decrease or increase of grey matter was shown in the fcMRI in autistic subjects in the ICN region, that is the frontal and temporal lobes (Zielinski et al., 2012). Injury to the brain impacts the volume and thickness of the grey matter. Zielinski et al. noted that grey matter increases in the frontal and temporal lobe affects communication and socialization. The decrease or increase of white matter were primarily found in the prefrontal lobe and temporal lobe of autistic

individuals (Zielinski et al., 2012) Similarly, discrepant white matter abnormalities have occurred in the corpus callosum.

The increase or decrease of neural interconnectedness may cause dense anomalies (Zielinski et al., 2012). Zielinski et al. (2012) showed co-existence of both over- and under-inter-connectedness. Some regions of the autistic center showed a lack of neural interconnection between regions. At the same time, other parts of the ICN system may show overabundance of neural interconnections. This type of overgrowth during early brain development in infancy has been identified in autistic individuals. There was distinct long-range underconnectiveness between regions, which implied that functionality of that area was compromised. According to Zelinski et al..autistic individuals had a distinct underconnectiveness between frontal and temporal regions.

Other issues with neural connectedness may result in blood oxygen level dependencies, which may indicate abnormalities in neural networks. The fcMRI data revealed that the canonical domain-specific, also known as the intrinsic connectivity network (ICN), had weaker neural network connectivity (Zielinski et al., 2012). The ICN typically showed strong network connectivity. The fcMRI test located altered areas in specific regions of the ICN. Diffusion Tensor Imaging (DTI), along with fcMRI, showed that the ICN's architectural structure was compromised in individuals with a tic. DTI is a diagnostic and tracking tool used for TBI (National Institutes of Health [NIH], 2013), and related to MRI. Unlike the traditional MRI, though, DTI can detect and monitor abnormalities in the brain's white matter, particularly the connections of nerve cells. DTI could indicate abnormalities in the ICN. Across the autistic center region, some areas

may have over- connectivity or over-growth, while others show underdevelopment or under-connectivity (Zielinski, 2012).

The fcMRI showed abnormalities in areas such as the prefrontal cortex, which regulates social and emotional functioning (Zielinski et al., 2012). The saliency network (SN), a part of the ICN, was comprised in ASD in a few structures, including the amygdala. Zielinski et al. (2012) found the SN underwent early degeneration in autism. This type of degeneration results in reduced activity causing the socio-emotional dysfunctions seen in autism. The SN also functions in integrating external stimuli and works to maintain homeostasis in order to stay alert or active. This involves integrating different systems, such as conflict monitoring, autonomic responses, and reward processing, which process information to help with decision making. A deficit such as injury in this region, causes information processing to be distorted. This type of distortion of information processing is also seen in autism (Zielinski et al., 2012).

Theory Relates to Study

Leo Kanner first formulated a theory of autism in 1940. He stated that autism is an impairment of specific functions, which is similar to the diagnosis of current ASD and its impairment of communication, social interaction and restricted/repetitive stereotypical behaviors (DSM-5, 2013).

Numerous theorists attempted to explain the possible causes of autism. Over a century ago, ASD was diagnosed as dementia praecox and hysteria (Kirby, 1908), infantile autism (Kanner, 1943), early infantile autism, childhood schizophrenia (Gibson, 1968), symbiotic psychosis (DeMyer et al.,1981), conduct disorder, mental retardation, autism, autistic disorder, pervasive developmental disorder and Asperger.

In the early 20th century, autism began to separate from childhood psychosis. In the mid-20th century, developmental factors, such as parenting style, were thought to cause early infantile autism. Much later, Folstein and Rutter (2006) conducted on early infantile autism and its correlation with brain injury. Folstein and Rutter explored parental educational status and socioeconomic status as etiologies of early infantile autism.

In 1911, Bleuler introduced the term *autism* in reference to schizophrenic patients (Chambers, 1969). Autistic symptoms were differentiated by the individual's altered state, comprising an inner life and the external world. Bleuler believed that the inner life dominates pathology. When this happens, the inner life is detached from reality (the external world), which resulted in autism. In the 1940s, Kanner was the first researcher to work directly with autistic children. This led to his term "early infantile disorder" (DeMyer et al., 1981, p. 392). This designation occurred while Kannr researched children with schizophrenia, but also noticed that the children were exhibiting unusual behavior. Kanner believed that autism was due to neuropathology and parent expectation stress (Gibson, 1968).

This etiology of autism was later considered as an organic factor. In 1970, organic factors such as a brain injury were also hypothesized as attributes of the antecedent to early infantile autism (Gibson, 1968). There was a wide range of organic factors that can cause other illnesses such as measles, encephalitis, convulsive disorders, fibroplasia resulting in oxygen tension, congenital temporal and frontal lobe disturbances, physiological and perceptual isolation, congenital stressors, degenerate encephalopathy, etc. Symptoms associated with these disorders are behavioral. There were no clear

biologically defined symptoms for young children that exhibit social impairments, communication impairments and stereotypical behaviors (Baieli, Paving, Meli, Flumara, & Coleman, 2003).

In the 1970s, Margaret Mahler contributed to the research on the causes of autism (Gergely, 2000) with a perspective based on separation-individualization theory, or the mother-infant attachment theory. Mahler had a psychoanalytical view of the psychological development of the infant leading to the developmental origins of adult psychopathology. Mahler adopted Freud's classical view of a closed system, which he described as an unhatched eggshell protective barrier. This was known as the stimulus barrier that shielded the infant from external stimulation. Mahler referred to this state as "normal autism," which she theorized occurred in the first two months after birth. The "autistic shell" is a "quasi-solid stimulus barrier" protecting the infant from external stimuli, thereby leaving the infant in an unresponsive state. In this case, if a disorder or disease persists, as well as an environmental insult or brain dysfunction, it could lead an infant to remain in an autistic state.

Literature Related to Key Variables and/or Concepts

The three key concepts examined are the domains of autism: socialization, communication and restricted/repetitive behaviors. These variables will be explored below.

Social interaction. Socialization was one of the three domains impacted in ASD. This study included measurement of socialization scores as a dependent variable. According to Radice-Neumann, Zupan, Baggage, and Willer (2007), individuals suffered from some level of social impairments, including interpersonal/social impairments. Some

of these social impairments are: inability to recognize the emotions of other people, interpreting another person's emotional state, avoiding or having difficulty resolving relationship issues, understanding another person's discomfort caused by difficult emotional states, comforting others adequately, recognizing facial expressions, and overcoming overall-impaired affect recognition.

Radice-Newman et al.(2007) addressed why social interaction was considered a signature trait of ASD. In ASD, social impairment was described as affecting emotional regulation, difficulty with emotion recognition, facial expression recognition, difficulty forming and maintaining positive relationships, social ineptitude, and some degree of emotional disengagement.

Radice-Newman et al. (2007) used a comparative study of neuroanatomical and behavioral findings. They conducted the study using a combination of archival data, computer-based generated data, software for data collection, neuroanatomical imaging, and existing ASD and brain injury treatment strategies. Radice-Newman et al. demonstrated similarities between neuroanatomical impairments and ASD. The review in these related studies was to examine the impact of injuries to parts of the brain that regulate socialization. The main factors influencing interpersonal social skills were emotion perception, recognition of faux pas (social awkwardness), empathy, and behavior. Radice-Newman et al. showed that neurological structures responsible for these social functions generally had an impact on social abilities. Damage to any of them created behavior similar to ASD.

Communication. Another variable examined in this study was communication difficulty. Communication scores on the ADOS-2 scales were used as a dependent

variable. The reason for its importance as a variable for this study comes from the possible relationship between age and gender and communication scores of ADOS. Rees and Bellow (2002) conducted their research on acquiring communication for the ASD population. The researchers used language impairments to demonstrate the similarities of language acquisition with ASD and focused on effective management of communications and skill-building in communication to point out communication flaws in ASD. Rees and Bellow used communication in their study because it was essential for individuals in recovery to regain confidence and regain inclusion in community life.

Rees and Bellow (2002) compared BI and ASD participants. They examined the effects of language and communication skills using four adult participants (men and women) with brain injury and were 2 years post-injury. Although the criteria of this BI population were to have functional and receptive language, the researchers reported that some individuals exhibited signs of ASD. These symptoms included severe disorders in communication, behavior and socialization.

Rees and Bellow (2002) used language and communication as independent variables. The dependent variables were the recording of language and communication skills observed at five levels. Similarly, this study had communication as an IV and the scores of communication test as the DV. The criteria Rees and Bellow used for the five levels of skills recorded are given below, with level 1 = the worst and level 5 = best performance. The recordings were captured at four different, consecutive contexts (site) ranging from C1- C4. C1 was the Baseline, C2 was the Camp, C3 was the Post-Camp, and C4 was the Follow-up. They found that language and communication production are shaped by a person's environment, regardless if they had ASD. Communication was a

struggle for ASD individuals. Flourishing language and communication skills determined the individual's level of effective communication. The researchers reported that the environment, site, and caretakers determine acquisition of language and communication. This was applicable in developing programs.

The five levels of communication noted above are:

Level 5, *Excellent and Positive Language and Communication*

· Consistent fluent and positive language and communication

· Consistent successful initiation and maintenance of interaction/conversation

· Total absence of socially inappropriate communication

· Total absence of interrupting behavior

· Correct understanding and response to cues

· Organized manner of expressions

Level 4, *Satisfactory and Acceptable Language and Communication*

· Mostly fluent and positive language and communication

· Mostly present initiation and maintenance of interaction/conversation

· Minimum use of socially inappropriate communication

· Minimum interrupting behavior

· Mostly correct understanding and response to cues

· Mostly organized expression

Level 3, *Equilibrium – potential for improvement or decline*

· Occasional fluent and positive language and communication

· Occasional presence of initiation and maintenance of interaction/conversation

· Occasional use of socially inappropriate communication

· Occasional interrupting behavior

· Occasional failure to correctly understand and respond to cues

· Occasional unorganized expression

Level 2, *Confused and Inappropriate Language and Communication*

· Frequent static and negative language and communication

· Frequent absence of initiation and maintenance of interaction/conversation

· Frequent socially inappropriate communication (not conforming with norms)

· Frequent interrupting behavior

· Frequent failure to correctly understand and respond to cues

· Frequent unorganized expression

Level 1, *Negative and Destructive Language and Communication*

· Frequent evidence of apathy/reduced motivation

· Frequent conversational/communicational indifference

· Reduced responsiveness

· Absence of communication-directed activity/non-communicative

· Frequent aggressive, destructive and/or negative language and communication

Restricted/repetitive behaviors. Another construct of interest examined in this study related to other peer-reviewed research and was restricted/repetitive and stereotypical behaviors. Nobile et al. (2011) explored this domain of ASD. The team wanted confirm if motor system dysfunction was a key domain of ASD, and to further examine the processing and integration of neural circuitry in repetitious/restricted or stereotypical skills. The researchers did a comparative analysis of ASD children and

healthy controls. They examined primarily gait parameters to determine if there was a significant difference between ASD and controls (Nobile et al., 2011).

Strengths and Weaknesses

Scientists have approached the etiology of ASD in numerous ways, from biological perspectives, genetic traits, sibling birth order, parental inducement, trauma, brain injury, immunization links, dietary interactions, teratogens, environmental problems, neuro-developmental disorders, and psychosocial problems.

The strengths inherent in the research involving ASD was its visibility and public appeal (Maino, Viola, & Donali, 2009). It touched the heart of the general public, and created a dynamic that contributed to funding research that increased the knowledge base of ASD, and greatly improved areas such as etiology, diagnosis, and treatment. Increased research led to more treatment facilities and created a new and fast-growing market for caregivers (Maino et al., 2009).

A second strength of such research was increasing the understanding ASD. Each ASD study has enhanced insights into this disorder. This further increases the call for a cure for ASD. ASD had shifted from once obscure condition studied by several fields to a commonly-used term (Maino et al., 2009). Many people now know someone who has ASD. As this condition begins in childhood, or was most pronounced during early childhood, ASD captured the public interest. It pulled on the heartstrings of families and communities. The dramatic push to raise awareness of this issue came from celebrities, traditional media, and social media (Maino et al., 2009).

The third strength was based on the theories of genetics and biological factors. The genetic theories helped to uncover that 30-40% of the ASD population was directly

tied to a genetic etiology (Schaefer, 2016). The other 60-70% of the ASD population had not been linked to any cause. This theory also identified the genetic susceptibility that involved the expression and phenotypic variability affected by the genetic changes seen in ASD. The proportion of phenotype attributed by genetic factors was estimated to be 0.07-0.09. The biological perspective involved research on the anatomy and physiology associated with ASD (Schaefer, 2016). Biological theory had offered the effects of environmental factors on childhood development and demonstrated how structures in the brain were linked to certain ASD behaviors (Schaefer, 2016).

The final strength was the theory that birth order had an association with ASD (Di Biasi et al., 2016). This theory suggested a recurrence risk of other siblings having ASD. Schaefer's study showed that 3 to 10% of ASD siblings had a recurrence risk compared to healthy siblings (2016). Recurrence was dependent on frequency and gender of the ASD sibling. When an older male sibling had ASD there was an increased risk for younger male siblings to have ASD. The frequency of ASD increased as the number of siblings rose. Although sibling birth order theory was still fluid, the strength of this theory was also the awareness of ASD during family planning (Di Biasi et al., 2016).

On the other hand, there were many weaknesses inherent in various theories surrounding ASD. One of the weaknesses was the cynical perspective that the subject has created an ASD Industry that provided a gold mine for researchers, pharmaceuticals, providers, and others who wanted to stake their claim and make a name for themselves. The media also plays a part in portraying autism as an epidemic, thereby creating more hype and a rush for a cure (Maino et al., 2009).

The second weakness was the intricacies of this disorder. ASD covers such a wide area of challenges, behaviors, developmental difficulties, and treatment variables that there cannot be a single cause. As Maino et al. (2009) wrote, it was a "monumental undertaking" (p. 151) to discover a single etiology for this disorder since it existed on a wide spectrum. Nevertheless, scientists continued to operate under the premise that they can find a single cause and cure. It is a convoluted topic due to its unpredictable nature, which created a challenge in the field of research. The dominant paradigm was to look at all the research and possible causes. This approach was inherently weak; it is called a spectrum for a reason. Looking for one answer was like asking, "What color is a rainbow?" The unique qualities of ASD demand a different approach to research. The current model tied several disorders together within ASD.

The final weakness identified for this study was the generally accepted focus on finding a cure. ASD is an Axis II disorder (APA, 2000). As ASD was not identified as a medical issue, it was not yet possible to map out a single process to formulate a cure. There may be multiple options to treating this disorder instead of a single method of preventing or curing it.

Rationale for Selection of Variables

There were two independent variables: age and gender. There were four dependent variables: three domain scores and a total score.

Independent Variables

There were two independent variables: age and gender (see Table 2) for the statistical test. The first independent variable was age and had four levels. Age was a variable because the onset of ASD varies. Using several levels of age group demonstrated

the impact of age on the scores. The second independent variable was gender because the prevalence of ASD in males is 4.7 times higher than that of females (ADDM, 2016). A way of quantifying the impact of gender on the ADOS-2 scores was attempted in this study.

Dependent Variables

There were four dependent variables, which were the scores measured by the ADOS-2 (see Table 2). The first three dependent variables were the domains scores: communication, socialization, and restricted/repetitive behaviors. The fourth dependent variable was the total score, also converted to severity scores, if necessary. The domain scores were chosen for analysis because they would show correlation between age, gender, and the scores on each domain. Similarly, total score demonstrated if there was a relationship between age and gender.

Total scores. Neuropsychological assessments were administered to diagnose or rule out autism based on the scores of the three ASD domains. This coincided with the ASD domains on the ADOS-2 for an individual to be diagnosed with autism. The total measure determined where on the spectrum the individual was functioning. Psychological testing determined if an individual was diagnosed with ASD using the total scores. However, this was converted to a severity score to determine the degree of functioning. There were divided into mild, moderate, or severe. The objective of the measure was to determine if the ASD criteria were met. The higher the score on the measure, the better the chance of being on the spectrum.

Communication scores. Communication, another major domain for ASD, was classified as verbal, nonverbal, or partial verbal (Rees & Bellow, 2002). These

individuals may or may not develop a small or selective vocabulary over their lifetime. All levels of verbal and non-verbal communications were noted in the data. In some cases, individuals used one to three-word sentences. In other cases, individuals might speak in short sentences. Some individuals are non-verbal, or partially verbal; they may grunt or sign. Others may have speech impediments. Some may speak in a repetitive manner, such as echolalia. This measure was used to determine if communication was impacted in ASD and if there was a correlation between the domains of the two instruments.

Socialization scores. According to the *DSM-5* (APA, 2013), socialization was a key component in diagnosing autism and was one of the three main domains affected by autism. Socialization can be defined as the natural ability to interact with another person. This is essential to human existence, as we are social beings. ASD individuals may be affected socially as follows: social ineptness, face repercussions, and they may not able to make or maintain friendships or strong relationships (Radice-Neumann et al., 2007). There may be different levels of social functioning affected by autism. Most individuals may not able to form lifelong bonds with friends or maintain intimate relationships. Some of these symptoms are: lack of interpersonal skills, not having friends, social isolation, and minimum interaction between friends or family, bonding only occurs with caretakers, no lifetime intimate partners, and social ineptitude. The socialization domain was used to measure ASD. The scores indicated if there was a deficit in this domain.

Scores on restricted/repetitive behavior. Restricted/repetitive behavior was among one of the traits of individuals affected by ASD. It was considered one of the three main areas of impairment (Nobile et al., 2011). Restricted/repetitive behaviors included

fluttering of the fingers, obsessive-compulsive behaviors, sensitivity to normal sensory stimuli such as light, temperature, sound, and touch. Stereotypical movements are based on neurologic deficiencies. The score on the measure of sensory/motor functioning domain was used as the DV measure. Impairment in this domain, as well as socialization and communication, was used as an indicator of ASD. The scores on this measure were taken from the ADOS-2 for individuals that have already been diagnosed.

Studies Related to the Research

Autism is a neurodevelopmental condition that is exhibited in behaviors. For this reason, it is theorized that it has a brain basis which affects behavior. Zielinski et al.'s (2012) research showed the region of the brain that corresponded to the symptoms of autism. Due to the specificity of the region, it is better known as the autistic center. My goal was to identify how the autistic center affects communication, socialization and repetitive/ restricted sensory behaviors.

The areas of the brain that are affected in ASD are the prefrontal cortex, cerebrum, basal ganglia, temporal lobe, Broca's area, amygdala, cerebellum, fusiform gyrus, and the corpus callosum. According to Zelinski et al. (2012), the list of structures and functions associated with ASD are numerous: Cerebrum (cerebral outer cortex) - motor activity, social and moral values; Basal ganglia - motor activity; Temporal lobe - speech, language, emotion, behavior; Broca's area - speech, language, communication; Amygdala - emotions, aggression, socialization; Cerebellum- speech and motor skills; Prefrontal cortex – affected emotion and social behavior; and the Corpus callosum– a relay system that integrates and communicates information between right and left hemisphere. (It generally relays sensory, motor, and cognitive performance.)

Although there are specific regions of the brain responsible for specific tasks, there are some interrelations between them. The brain is a neural electrochemical circuit. The neurons form a network that is meshed or interconnected (Zielinski et al., 2012). This sometimes leads to overlapping of neurons in different structures. Speech functions reside in multiple centers such as the temporal lobe, Broca's area, the cerebellum, etc. However, communication appears in the Broca's area and an associated communication capacity (relaying information) that functions via the corpus callosum. Similarly, the temporal lobe, cerebellum, and Broca's area may work together to form congruent statements. When a task was initiated, such as a response to a question, the different regions of the brain (communication, speech, language, emotions, memory, etc.) may be collectively activated to answer the question. Thus, the ability to understand, analyze, and speak a full sentence requires numerous areas to produce a response. Basically, the temporal lobe, Broca's area, cerebellum, and corpus callosum, must all be connected to enable one to speak and communicate effectively. Any impairment to these areas may affect communication.

Autistic children do not generally communicate effectively (Janzen, 1996). Children may understand language, but cannot speak and are considered nonverbal. There are also children who can speak a language, but cannot articulate and communicate effectively. An example of this is when someone suffers from echolalia, which is due to interference in the communication process. Individuals with echolalia repeat what others say verbatim. This creates a situation in which a child speaks the words but cannot analyze or understand what is being said. Non-autistic children may go through a period of echolalia and they repeat what others say. But, if they are asked a question, they

attempt to answer. In autistic echolalia, children respond to a phrase, statement, or question by repeating the last phrase, question, or sentence and do not answer the question. This indicates possible impairment in the brain region for communication. Therefore, this type of impairment could be a developmental delay in communication for autistic individuals.

Another relevant theory relating to this study was information acquisition, and cognitive and psychological development (CPD) (Mundy, Gwaltne, & Henderson, 2010). CPD theory was developed by Jean Piaget (Papert, 1999) and attempted to explain how information was processed in the brain. The theory was relevant to this study because injury to the brain could lead to impairment in CPD, which resembles ASD. The key concept of CPD was the individual's ability to process information passively acquired from the environment. Injury to the brain could affect acquiring and processing such information. Similarly, autistic symptoms included an impaired ability to acquire and process information. BI, such as TBI, was shown to be the leading cause of acquired disability, such as CPD impairments (Chevignard et al., 2010).

If the injury occurred in the ICN region, it may cause autistic-like symptoms (Zielinski et al., 2012). The specific domains of autism were communication, socialization, and restricted/repetitive behaviors. If the injury affected these domains collectively, it may appear as ASD.

Gap in Literature

The gap in the literature was the lack of information supporting a direct link between age and gender, and the numerous neurodevelopmental disorders across the autism spectrum. There was no known research directly addressing age and gender

comparing the neurodevelopmental functioning of ASD using the ADOS-2 measure. There were multiple theories about autism including some empirical support for a genetic link to autism. The criterion for autism was not directly a physical disability, because it is a neurodevelopmental disorder, which may impact cognitive functioning and possibly physical motor-sensory abilities.

Zielinski et al. (2012) supported the theory that a deficit in neurological functioning of the brain may be caused by abnormalities and/or injuries. However, there was no literature giving a neurodevelopmental basis related to age and gender in ASD. The gap in the literature was that there was not enough evidence to show that age and gender correlated with neurodevelopmental components. A correlation between age and gender and these components was sought, and differences in age played a role in the severity (total ADOS-2 score) between age groups and gender. Also, the fact that domain component scores addressed age and gender performance was shown by the research. There was no literature that directly supported this outcome. This gap in the literature led to further research on specific populations with ASD.

Summary and Conclusion

In this chapter I provided background on various studies relating to autism. Researchers explored various ASD theories to support the premise for this study. ASD is a neuro-developmental disorder with a steadily increasing prevalence in the U.S. (ADDM, 2016). The purpose of this current study was to examine how differences in age and gender were related to total score and domain scores of communication, socialization and restricted/repetitive behaviors of ASD, as measured by the ADOS-2.

In the literature review I focused on the impact of age and gender on neurological and neurodevelopmental approaches to ASD. The neurological theory integrated anatomy and physiology into the development of ASD. Neurodevelopmental theories examined were on the progression of ASD by age and gender. Various studies were synthesized to demonstrate the purpose, background, and design of this current study. In the following chapter I elaborate on the study's methodology.

Chapter 3: Research Method

The purpose of this study was to examine how the differences in age, and gender are related to the total and domain scores of communication, socialization and restricted/repetitive behaviors of ASD, as measured by the ADOS-2. This was a quantitative research design in which I addressed the relationship between the independent and dependent variables. This current research design utilizes archival data with sample size of eighty.

The statistical tests I used for this study were the MANOVA and 2-way ANOVA. The MANOVA tested for the difference in domain scores based on age and gender. The 2-way ANOVA tested for the differences between age and gender and total scores. There were two independent variables for the statistical test: age groups and genders and four dependent variables (i.e., three domain scores and total score).

This chapter includes the various inquires of scientific method used for data collection and the selection style of population. The methodology section includes an outline of the population and sampling techniques. This chapter includes a detailed process of the procedures used for data collection. All permissions and requests obtained for the methodology, such as Institutional Review Board of Ethical Standards in Research (IRB, 2017), the NIMH-NDAR (2015), and any other pertinent documents, were filed in the appendices. The instrumentation and operationalization of variables are provided later in this chapter, along with the topic on threats to validity. In the ethical procedures section of this chapter, I addres how data were obtained in an ethical manner, along with the IRB process for obtaining their approval.

Research Design and Rationale

I used a quantitative research design using archival data to conduct a comparative analysis method. The research design included two independent variable groups: age (four) and gender (two). There were four dependent variable groups: one total score and three domain scores on socialization, communication and restricted/repetitive behavior. I slected a quantitative method for this current study because, as Creswell (2009) noted, it provided a description of the relationship between the variables and a comparison of the scores. A quantitative research design was also chosen because the variables can be measured and quantified into a numeric and categorical format. I used the ADOS-2 in this study. The ADOS-2 scores were from the archival data from the federal government, NIMH-NDAR (2015). Administrators of the ADOS-2 must be trained and certified to give this test, and they are primarily licensed psychologists. Because the groups within the study cannot be manipulated or randomized, the quasi-experimental approach was the most appropriate. This quantitative method was more appropriate than either a qualitative or mixed methods approach because it allowed for the quantifiable performance of participants' responses.

Methodology

Population

The sample population was individuals with ASD. The parameters for this sample were children and adults previously diagnosed with ASD and assessed with the ADOS-2. A sample size of 80 was taken from the NIMH-NDAR (2015) archival data. The data set used consisted of thousands of participants tested for ASD using the ADOS-2 assessment. The selected 80 participants were chosen and semi-randomly placed into four

categories, which were based on age and gender. All participants were diagnosed with ASD. NIMH-NDAR granted permission for this data collection. Therefore, ASD individuals in the program had to be officially diagnosed. For individuals with an ASD diagnosis, their level of functionality fell anywhere in the ASD range. Whether their level of impairment was mild, moderate or severe, they still qualified to be within the sampling parameter.

The sample was based on participants diagnosed with ASD. The sample was pulled from a pool of ASD population. The participants used for this current study have been diagnosed with ASD via the ADOS-2. This is a stratified random sample, which was categorized by age. Another random sampling selection was used to categorize the gender. Demographics and characteristics such as age and gender and ADOS-2 scores were obtained from the data set. The scores and demographics were extracted and used for statistical analysis for this study (see Table 2).

Table 1

Data from Individual Case Record File

IV/DV	Domain Scores Com/Soc/RRB	Total Scores
Gender		
Male		
Female		
Age (years)		
1 - 4		
5 - 8		
9 - 17		
18 – Older		

All participants selected had an ASD diagnosis. The children and adolescent participants were under 18 years of age. The adult population were 18+ years of age. This age groups were: 1-4, 5-8, 9-17, and 18+. The individuals were primarily selected due to their ASD diagnosis, ADOS-2 testing, and thier age and gender.

Sampling and Sampling Procedures

The statistical tests used for this study were the MANOVA and 2-way ANOVA to determine the relationship between age, gender, and domain scores and total scores. There were four dependent variables: three of domain scores (communication, socialization, and restricted and repetitive behaviors) and the total scores. There were two independent variables: age and gender. The MANOVA and ANOVA with an effect size of $f^2(V) = 0.50$, calculated a sample size of 80 with power = .99, and significance level= .05.

Sample size: Selection of power (1 - β) and significance level (α). The sample size for this study consisted of individuals having ASD drawn from an archival pool. The individuals selected had all taken the ADOS-2. The sample size was selected via a power analysis using the statistical calculator, *G*Power Software 3.1.7* (Faul, 1992-2012). The statistical significance level used was $\alpha = .05$. The calculation for the proposed research gave a minimum sample size, which was achieved by a standard minimum power of $1 - \beta = .95$. However, by increasing the standard of power to $1- \beta = .99$, a larger maximum sample size resulted. The range allowed for no less than the minimum sample size but could exceed the maximum. This was done in this study.

Effect Size $f^2(V)$. For this study, I obtained the average effect size using three studies on autism. The effect size [$f^2(V)$] was interpreted according to the Cohen's (1988)

descriptive guidelines with a small effect =.2, medium effect=.5, and large effect= .80. For the first study, I used the effect size because the population had a diagnosis of ASD (Dodd, Ocampo, & Kennedy, 2011). ASD students with a pre- and post-test for language intervention were examined in their study. The average effect size from small to large was $f^2(V) = .69$.

Subramanian, Huai, and Weisner (2011) measured ASD domains. The effect size for these studies from small to large had an average of $f^2(V) = .78$. The final study by Cicchetti et al. (2010) measured ASD domains from a small to large effect size has an average of $f^2(V) = .60$. The calculated average effect size of the three studies of related peer review was $f^2(V) = .72$). Because the G-factor was more limiting when the sample size was limited, I utilized Cohen's medium size. Therefore, the effect size selected for this study used Cohen's average effect size of $f^2(V) = 0.50$. A maximum sample size of 68 resulted for both tests.

F-test analysis: MANOVA. I used MANOVA to examine the difference between two independent variables and four dependent variables (Faul et al., 2009). The two independent variables for the MANOVA are age and gender. The dependent variables were the total and domain scores (socialization, communication and restricted/repetitive scores). The test family for MANOVA was the critical value *F* test. The statistical test used was the MANOVA: fixed model, R^2 increase. For the MANOVA, I used an average effect size of $f^2 = .50$, per Cohen's (1988) medium effect size.

The test of power analysis was the *a priori* power analysis for the MANOVA. The critical *F*-test was selected with a level of significance of $\alpha = .05$. The standard of power used was $1\text{-}\beta = .99$, which provided the sample size of 52. The relationship

evaluated at α = .05, with the power of 1-β = .95, the effect size of f^2(V) = .50, resulted in the critical value F = 2.2346, and the calculated sample size is 52.

F-test Analysis: 2-way ANOVA. The ANOVA determined the relationship between two and four variables and four dependent variables (Faul et al., 2009). The two independent variables for the MANOVA are age and gender. The dependent variables were for the total and domain scores. The test family for ANOVA was the critical value *F*-test. The statistical test used was the ANOVA: within-between interaction. For he MANOVA, I used an average effect size of f^2 = .50, per Cohen's (1988) medium effect size.

The test of power analysis was the a priori power analysis for the ANOVA. The critical *F*-test was selected with a level of significance of α = .05. The standard of power used was 1- β = .99, which provided the sample size of 16. The relationship evaluated at α = .05, with the power of 1- β = .95, the effect size of f^2(V) = .50, resulted in the critical value F = 3.3404, and the calculated sample size was 16.

Based on the aforementioned parameters, the calculated sample size between the two tests were 16 and 52. To maintain consistency between the two powers, the maximum sample size chosen to be used for this current research was 52. However, to provide robustness for various tests, Iutilized 80, which was beyond the maximum required from the sum of the two tests.

Procedures for Recruitment, Participation, and Data Collection

NIMH-NDAR, used for archival data, granted permission for this study to collect data after approval from the Walden IRB (2017). I did not have direct contact with the ASD participant; therefore, informed consent was not needed. The participants'

information is de-identified or decoded. The data collected for variables analyses included demographics such as age, gender, total (severity) scores and domain scores (communication, socialization and restricted/repetitive behaviors).

Data collection procedure. The data collection process occurred in four phases.

Phase 1:

- I submitted IRB approval after approved proposal and approved oral defense.
- The IRB returned application form to me. The IRB requested that I submit source of data collection.
- I submitted a request to NIMH for Data Repository Data Use Certification (DUC). The DUC form had detailed information about this study, its methodological design and its purpose.
- NIMH returned the DUC seeking Walden Grants Department permission for the data collection from NIMH.
- I hired Dr. Lauck from Walden Grants Department to assist with the NIMH data collection process.
- Dr. Lauck advised research on the DUC process. STEP 6: Accordingly, I contacted the NIMH helpdesk to determine if the relevant data were housed in NIMH-NDAR database and then resubmitted the IRB application.
- The IRB granted pre-approval for data collection with the conditions of NIMH approval.
- I submitted the IRB preapproval to Dr Lauck.

- Dr. Lauck granted permission for NIMH-DUC.
- I subsequently resubmitted DUC to NIMH for data collection.
- NIMH granted approval for DUC on the NDAR database.
- I sent NIMH's approval to the IRB.
- IRB granted final approval for this study.

The following steps were conducted during Phase 2.

- After IRB final approval, I began the data collection process.
- I contacted NIMH helpdesk to assist with the data transfer.
- I downloaded the relevant data from the NIMH-NDAR data set. The sample pool was selected from participants that ware all given the ADOS-2 assessment. The data sets were categorized by module, which is aggregation of ADOS-2 scores by age.

Phase 3 was the beginning of the data collection process.

- I scanned through the data sets or participants identifying information. All the participants' information was deidentified, which qualified the data collection process to be in accordance with the HIPAA privacy act.
- I reviewed the data set for the following information: ADOS-2 total scores, ADOS-2 domain scores, ADOS-2 total (severity) scores, and demographic information (age and gender).
- I categorized the data set by age. This categorization of data was based on four age groups: Group 1 (1-4 years), Group 2 (5-8 years), Group 3 (9-17 years) and Group 4 (18 years and older). Each participant's information

(within the module) was not listed in any particular order of age or gender).

- Within each category (module), I filtered the participants' data that were only ASD diagnosed.
- Participants were now categorized by ADOS-2 assessment, four age groups, and ASD diagnose. STEP 21: within each age group (four groups), the participants were further sorted from youngest to oldest.
- Within each age group (with a range of years), the participants were selected to ensure diversity in age.
- The participants were selected by gender to match the year as close as possible for both genders.
- The final selection process was to ensure all three domains' scores were present.
- The data were selected, coded and populated into a spreadsheet.

Phase 4, the final steps, consisted of:

- I started the statistical analysis.
- Interpreted the data and deduced the findings.
- I reported the findings in Chapter 4.
- After completing Chapter 4, I encrypted and saved NIMH-NDAR data set for 5 years.

Instrumentation and Operationalization of Constructs

All participants were diagnosed with ASD using the ADOS-2 tool. The primary information collected for this study was demographic (age and gender), domain scores

and total scores. Archival data from the diagnostic test, ADOS-2, was used. The reliability and validity values of the ADOS-2 instrument used from the archival data are addressed later in the chapter.

Instrumentation

The instrument used for this study was the ADOS-2. The groups used for the independent variables are ASD participants diagnosed with the ADOS-2. Age and gender are the independent variables. The scores on the ADOS-2 test were used as dependent variables.

ASD is not a diagnosis of a definitive pathology, but a psychiatric diagnosis supported by the *DSM-5* (Falkmer, Anderson, Falkmer, & Horlin, 2013). Given that there is no blood test or scan to diagnose ASD, the only tools for diagnosing are neuropsychological assessments to evaluate the symptoms of ASD. The ADOS was among the most reliable tests for diagnosing ASD. The ADOS-2 instruments are evidence-based and considered the standard. The ADOS-2 has the highest sensitivity and specificity among ADS diagnostic instruments. Most other ASD instruments were not solely reliable as ASD diagnostic tests, except if used in conjunction with either the ADI-R or ADOS-2. The ADOS-2 was considered an ASD diagnostic instrument that demonstrated correct classification rates of .85 and .80.

ADOS-2 standardized test. The first ADOS instrument was introduced in the 1980s (Lord, Rutter, DiLavore, & Risi, 1999). The ADOS-2 was revised in 2012 (Lord et al., 2012) and is a standardized assessment considered the gold standard of ASD diagnostic instruments. It is considered a semi-structured observational instrument used

to assess communication, reciprocal social interaction, imagination/creativity, stereotyped behaviors, and restricted interests for diagnosing autism spectrum disorders.

Validity and reliability. Falkmer et al. (2013) conducted a study of the ADOS-2. They addressed the accuracy, reliability, validity and use of ADOS as a diagnostic tool. They also compared ADOS with 17 other tools, and the ADOS stood out as having the highest sensitivity and specificity. Sensitivity was 0.87, specificity was 0.78, and the correct classification was 0.82. Cronbach's alpha coefficient was 0.70. The inter-rater reliability for ADOS-2 exceeded 80% (Haus & Lord, 2014). Item agreement was initially established at 80% and consistently exceeded 75%.

According to the ADOS-2 manual (2012), the internal consistency (as measured by Cronbach's alpha) of the ADOS-2 overall scores ranged from fair to excellent (.60-.95). Inter-rater reliability was good (0.90-0.96), and test-retest reliability was fair to good (.64-.92). The domain component scores of the ADOS-2 module showed internal consistency, as measured by Cronbach's alpha (Haus & Lord, 2014). Socialization and communication alpha was .84 and the restricted/repetitive behavior alpha was .61. Gotham, Risi, Pickles, and Lord (2007) used the revised ADOS-2 to determine its diagnostic and predictive validity. They found there were improved diagnostic validity compared with the original algorithms. Gotham et al. also reported that the improvement in predictive validity was apparent. The ADOS-2 elicits particular tasks (Lord et al., 1989). The inter-rater reliability for five raters exceeded the weighted kappas of .55 for each item. The test-retest reliability was high; discriminant validity was also high.

Administration. The administration of the ADOS-2 assessments was observationally-based, in that the individual was evaluated through observation of

activities and play, and not interview (Gray, Bruce, Tonge, & Sweeney, 2008). The clinician used toys and activities specific to the assessment to elicit responses for social and communicative interaction with the individual. The response was coded as absence or presence of desirable responses. The performance of the individuals was coded with scores that indicates normalcy or abnormality. The higher scores represent a higher likelihood of an ASD diagnosis. The diagnostic algorithm consisted of the domains of communication, reciprocal social interaction, play, imagination/creativity, and stereotyped behaviors and restricted interests.

There are five modules in the ADOS-2 (Lord et al., 2012): Toddler and Modules one through four. Each module required the clients' demographics. The modules are primarily based on chronological age, expressive language level, and verbal fluency. Each module had observational and coding scales. The modules had scoring sheets with several sections. The sections were the conversion of scores into algorithms, the level of functioning (severity) classification, and the diagnostic section.

The toddler module was for children between the ages of 12-30 months (Luyster, Gotham, & Whitney, 2009). The toddler module (Module T), was designed for this age group due to a lack of consistent use of phrase speech. Module T screens for pre-verbal and single-word performance. Module T had 11 observational items with four sub-items. For the coding scale, there were three categories. The first is Scale A, the second was for language and communication, and the third had nine scales.

The first four modules were among the ADOS-2 revisions by Lord et al. (2012). Modules were all observational and scoring was categorical. Results were recorded with numeric codes. Scoring was based on chronological age. The following is an example of

Module one, age 31 months and older:

The numeric categories are:

0 = Regular use of utterances with 2 or more words; points with finger for visual references; spontaneously give object to others; movement appropriate.

1 = Occasional phrases only; points with finger for visual reference but with limitations; mostly single words; one gave object to others; rare disruptive movement.

2 = Recognizable single words or word approximations only; points to object but with no visual gaze; must use at least five different words during the ADOS-2 evaluation; rarely or never give objects to others; fidgets.

3 = At least one word or word approximation, but fewer than five words used during the ADOS-2 evaluation; does not point; not engaged; marked disruptive movement.

4 = No words or word approximation used meaningfully.

5 = Not meaningful.

6 = Unusual but not quite excessive.

7 = Usually frequent, intense, or excessive demands for attention.

8 = N/A; No echolalia noted; language too limited to judge; severe motor difficulties.

These codes were later converted into numeric scales for severity conversion and diagnostic classifications. The coding indicated the severity of the impairments from zero to eight, with zero being mild and eight most severe. Severity was measured by the comparison score, which corresponded to the individual's age. An example was based on

age 31 months and older, which was shown above in Module one.

ADOS-2 comparison scores range from zero to ten based on the level of severity that corresponds to age. For example, Module one, for 31 months and older, is scored as follows. Scores of zero to two are minimal to no evidence of ASD or related symptoms. Scores of three to four are low severity; five to seven show moderate severity, and eight to ten indicate a high level of severity.

The coding for the ADOS-2 diagnostic classification measures symptoms along the range of ASD, depending on age. For example, using Module 1, classification is coded by number of words with a score between seven and sixteen. Assigning ASD is classified as autism, autism spectrum, and non-spectrum autism disorder (levels 12-16 overall total). The autism spectrum disorder is between levels eight and 11. The non-spectrum or related is from seven to 10. The overall total score is less than that of the autism spectrum.

Module one was for individuals 31 months and older. This module test is for pre-verbal and single words (Gray, Tonge, & Sweeney, 2008). In comparing autistic versus non-autistic participants, sensitivity was 1.00 and specificity was .79. Module one has 10 items for the observational scale. Under the coding scale are five sub-scales (A-D). Scale-A measures language and communication and has eight items. Scale B measures reciprocal social interaction and contains 16 items. Scale C measures play and has two items. Scale D measures stereotyped behaviors and restricted interest and has four items. Scale-E measures other abnormal behaviors and has three items.

Module two was for children and adolescents that used phrase speech but were not verbally fluent (Lord et al., 2012). The sensitivity for this module is .95 and

specificity is 0.73. Module two has 14 items under the observational scale. There were five coding scales (A- E). Scale A is language and communication having seven items. Scale B is reciprocal social interaction with 12 items. Scale C is for play and has two items. Scale D is for stereotyped behaviors and restricted interests having four items. Finally, scale E is for all other abnormal behaviors that had three items.

Module three is designed for a children and adolescents fluent in speech (Lord et al., 2012). The observational scale has 14 items. There are five coding scales (A-E). Scale A is language and communication, with nine items. Scale B is for reciprocal social interaction (11 items). Scale C is for play with one item. Scale D is for stereotyped behaviors and restricted interests (five items). Scale E is for all other abnormal behaviors (three items).

Module four is for older adolescents and adults with fluent speech (Lord et al., 2012). Module four of ADOS-2 was further updated (Haus & Lord, 2014) but maintained its name as ADOS-2. The update was for the algorithm of verbal fluency and severity scale. This module has 15 items on the observational scale; five items were optional. There are five coding scales (A- E). Scale A is language and communication (10 items). Scale B is for reciprocal social interaction (11 items). Scale C is for play, with one item. Scale D is for stereotyped behaviors and restricted interests (five items). Scale E is for all other abnormal behaviors (three items).

Operationalization

The operational definition used for the independent variable was the groups of individuals categorized based on their diagnosis of ASD: age and gender. The operational definition for the dependent variable was the total scores and domain of ASD, which

were communication, socialization, and restricted/repetitive behaviors. Eighty individuals were selected from the archival data set that fitted into the ASD group and constituted the ADOS-2 group.

ADOS-2 Groups. The two groups of independent variables were age and gender. The four dependent variables were total and domains scores from the ADOS-2. The ADOS-2 test was used to measure the performance on ASD domains. The three domains measured by ADOS-2 correspond to the ASD domains of communication, socialization and restricted/repetitive behaviors (see Table 6). The scorings were recorded separately. ADOS-2 domain scores were numeric and total scores, when converted to severity scores, were categorical. The range of the total scores were recorded as a range of numbers for total scores and then converted to severity categories. The severity categories were: 1 = mild, 2 = moderate, and 3 = severe, which were derived from the total scores. However, the severity scores were converted into standardized scales, which allowed for severity comparison scores and diagnostic classification.

As this study used archival data, the scores collected were secondary data, based on previously administered tests. The three measures (communication, socialization, restricted/repetitive behaviors) represented impairment of neurodevelopmental components in ASD. For example, when looking at the domain of socialization interaction, the scores were represented by descriptive data. The raw scores collected were organized into a range of numbers. Age and gender were also in the assessments, which were collected as categorical and numerical data, which converted into discrete variables. The three categories of ASD level of functioning were mild, moderate and severe. These categories were also used to designate the level of functioning and

diagnostic criteria for ASD. Therefore, when collecting the data, the participants' records already indicated a severity category of mild, moderate, or severe.

Data Analysis Plan

Data were entered into the *Staistical Package for the Social Sciences* (SPSS), *version 22.0 for Windows* for analysis. Descriptive statistics were presented to describe the characteristics of the sample, and their scores (see Appendix C). Categorical data were presented for age and gender, which I converted into discrete variables. Means and standard deviations were presented for continuous and categorical data.

The data were screened for missing cases and outliers. Univariate outliers were assessed for the three research variables: socialization interaction scores, communication scores, and restricted/repetitive behavioral scores. Univariate outliers were also examined via standardized values (*z* scores), where standardized values below -/+3.29 are considered outliers (Tabachnick & Fidell, 2012). As the data were categorized, the outliers were placed into the mild or severe range. The three scores were assessed for normality using Kolmogorov-Smirnov (KS) tests; one KS test per score. The absence of multicollinearity among the three scores was assessed via Pearson correlations, whereas correlation above .90 indicates the presence of multicollinearity (Tabachnick & Fidell, 2012). Statistical significance for the KS test for normality and the correlations for multicollinearity was used to determine whether there was an alpha value of .05. The data collected were interpolated for significance.

Research Questions and Hypotheses

The hypotheses and the research questions for this study are stated below:

Research Question 1. Are there age and gender differences in ADOS-2 domain

scores of socialization, communication, and repetitive/restricted behavior?

$H_0$1: ADOS-2 domain scores of socialization, communication and repetitive/restricted behavior do not differ by age (categorical variables; ages 1-4, 5-8, 9-17, 18 and older) and gender.

$H_1$1: ADOS-2 domain scores of socialization, communication and repetitive/restricted behavior differ by age (categorical variables; ages 1-4, 5-8, 9-17, 18 and older) and gender.

TEST: MANOVA was used to run this analysis.

Research Question 2. Are there age and gender differences in the ADOS-2 total scores?

$H_0$2: The ADOS-2 total scores do not differ based on age and gender.

$H_1$2: The ADOS-2 total scores differ based on age and gender.

TEST: ANOVA was used to run this analysis.

Ethical Procedures

IRB Application and Access to Individuals

Agreements to gain access to individuals or data were done through the IRB application (2017). Although the data sample was archival (de-identified data), the sample population was categorized as a specialized population, which consisted of individuals with developmental disabilities, children, and various other special needs. Archival data were chosen to avoid privacy concerns about the data. No interaction or contact with members of the studied population took place. The treatment toward humans was not applicable, as it was archival data. Data were reviewed only through a database containing de-identified information. NIMH and Walden's IRB granted permission to

collect pertinent data, which was limited because NIMH provided the restricted information.

Treatment to Human Individuals

Permission was granted by NIMH-NDAR to use archival data from a population diagnosed with ASD. Permission from Walden's IRB was sought and granted as well. Eighty participants were used in this study. These individuals were not recruited because this study utilized only archival data. Data were randomly and non-randomly chosen from the relevant dataset.

The files from the NIMH database that were extracted from NIMH are to remain with the researcher in a safe and private place, stored according to the privacy provisions of the *Health Insurance Portability and Accountability Act of 1996* (HIPAA). There was a possibility that there may have been ethical issues during review of database, such as identifying information being revealed. I reviewed the datasets for identifying information and found no privacy concern.

Treatment of Data

There was no identifying information of participants provided by NIMH. The data collected from the agency is archival. Identifying information was not shared or communicated. Secure storage was used to store the data according to HIPAA provisions. For purposes of data security, the datasets collected for this study were encrypted and will be stored for 5 years, after which all information will be deleted.

I have had no relationship with NIMH. I have had no employment history with NIMH or access to identifying information of participants. No incentive measures were used, as all the information collected were limited to archival data. No staff, nor

employees of NIMH were compensated in any way for their services pertaining to the study.

Summary

I designed this study to investigate the unknown nature of 60-70% of the unknown nature of ASD origin. The purpose of this study was to examine how age and gender are related to total scores and domain scores of communication, socialization and restricted/repetitive behaviors of ASD, as measured by ADOS-2. The research questions and hypotheses were written to investigate a sample with ASD, as confirmed by using the ADOS-2. Statistical tests used were the MANOVA and two-way ANOVA. Their purpose was to examine if there was a difference between age and gender, and that of total scores (severity) and domain scores. The significance of this study was that it advanced the knowledge base concerning age and gender differences on the neurodevelopmental functioning of individuals with ASD.

In this chapter, I described the research design. The method used was a comparative quantitative design using archival data. The sample population was selected from the NIMH-NDAR database. NIMH and Walden's IRB granted written permission for data collection. The data collected were numeric and was also categorical.

The data collection process will be presented in the following chapter. This chapter was based on data being collected, organized, calculated, analyzed, interpreted and reported. Chapter 5 consists of the discussion, recommendations and conclusion of the study.

Chapter 4: Results

The purpose of this current study was to examine how differences in age and gender of those diagnosed with ASD are related to total scores and domain scores of communication, socialization and restricted/repetitive behaviors, measured by ADOS-2. A quantitative research design (n = 80) with two independent variables: age (ages 1-4, 5-8, 9-17, and 18-older), and gender (male and female) was used. The four dependent variables were the domain scores and the total score measured by ADOS-2. The statistical analyses used were the MANOVA and 2-way ANOVA, which determined differences for by age and gender for the domain and total scores.

Data Analysis

The data were imported into SPSS from *Microsoft Excel* for analysis. The independent variables were age (four levels) and gender (two levels). The dependent variables we total scores and three domain scores. I used MANOVA to test for the predictive relationship of age and gender, on domain scores of the ADOS-2. I also used a 2-way ANOVA to examine the relationship between age and gender, and the total scores of the ADOS-2. I assessed the assumptions of the statistical tests before statistically testing the hypotheses and summarized participants' demographic data.

Participant Demographics

All participants (n = 80, 100%) had a diagnosis of ASD. Age ranged from 1-44 years with a mean of 11.5 years (SD = 112.68). As seen in Table 3, participants were evenly distributed between the age groupings, with 20 in each: 1-4 years (n = 20, 25%), 5-8 years (n = 20, 25%), 9 – 17 years (n = 20, 25%) and 18 years and older (n = 20, 25%).

Table 2

Frequencies and Percentages for Participants' Demographics (N = 80)

Variable	*N*	%
Age Group		
1-4 years	20	25.0
5-8 years	20	25.0
9-17 years	20	25.0
18-older	20	25.0
Total	80	100.0
Gender		
Male	41	51.0
Female	39	49.0
Total	80	100.0

Descriptive Statistics

The descriptive statistics for the dependent variables appear in Table 4. Communication (Com-C) scores ranged from 1 to 6 with a mean of 2.16 (*SD* = 1.08). Socialization Interaction (Soc-S) scores ranged from 4 to 22 with a mean of 12.83 (*SD* = 4.66). Restricted/Repetitive Behavioral (RRB-R) scores ranged from 1 to 10 with a mean of 4.40 (*SD* = 1.92). Total (SR) scores ranged from 9 to 32 with a mean of 19.63 (*SD* = 5.85).

Table 3

Descriptive Statistics for the Dependent Variables (N = 80)

	Min	Max	Mean	*SD*
Communication (Com-C)	1	6	2.16	1.08
Socialization Interaction (Soc-S)	4	22	12.83	4.66
Restricted/Repetitive Behavioral (RRB-R)	1	10	4.40	1.92
Total (CSR)	9	32	19.63	5.85

Preliminary Analysis

Univariate outliers were assessed for the dependent variables: socialization interaction scores, communication scores, and restricted/repetitive behavioral scores. Univariate outliers were examined via standardized values, or *z* scores, where standardized values below -/+3.29 are considered outliers (Tabachnick & Fidell, 2012). No outliers were identified. The absence of multicollinearity among the three scores were assessed via Pearson correlations, where any correlation above 0.90 indicates the presence of multicollinearity (Tabachnick & Fidell, 2012). There was no multicollinearity found. As seen in Table 5, there was one statistically significant correlation, between Socialization Interaction and Restricted/Repetitive Behavior ($r = .34$, $p < .01$) but the correlation was moderate; the assumption of a lack of multicollinearity was met.

Table 4

Analysis of Multicollinearity for the Dependent Variables Using Two-Tailed Pearson Correlations (N = 80)

		Communication (Com-C)	Socialization Interaction (Soc-S)	Restricted /Repetitive Behavioral (RRB-R)
Communication (Com-C)	*r*	1		
	p			
Socialization Interaction (Soc-S)	*r*	.11	1	
	p	.32		
Restricted/Repetitive Behavioral	*r*	.02	.34**	1
(RRB-R)	*p*	.83	.002	

Note. ** indicates the correlation is significant at the .01 level (2-tailed).

Multivariate outliers were assessed using the Mahalanobis distance. The maximum Mahalabonis distance for the sample was 13.54. The critical value for three dependent variables was 16.27 (Tabachnick & Fidell, 2012); thus, I concluded that there were no substantial multivariate outliers. The homogeneity of variance-covariance matrices was tested using Box's *M* test of equality of covariance matrices in the MANOVA procedure and it was not statistically significant ($p = .75$, see Table 6).

Table 5

Box's Test of Equality of Covariance Matrices

Box's M	*F*	*df1*	*df2*	*p*
41.45	0.84	42	8400.70	.75

Note. Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

Normality was tested using the Kolmogorov-Smirnov test. As seen in Table 7, the test was not significant for the overall total scale but significant for the domains, which suggests that the domain scores were not normally distributed.

Table 6

Test for Normality

	Kolmogorov-Smirnov		
Variable	Statistic	*df*	*p*
Communication (Com-C)	.20	80.00	.00
Socialization Interaction (Soc-S)	.11	80.00	.01
Restricted/Repetitive Behavioral (RRB-R)	.15	80.00	.00
Total Score	.09	80.00	.19

Although the significance tests of MANOVA are based on the multivariate normal distribution, in practice it is reasonably robust to modest violations of normality (except where the violations are due to outliers). According to Tabachnick and Fidell

(2007), a sample size of at least 20 in each cell should ensure robustness. Both independent variables fulfill this requirement so it was appropriate to perform the MANOVA.

Results for the Research Questions and Hypotheses

Research Question 1

Research Question 1 was: Are there age and gender differences in the ADOS-2 domain scores of socialization, communication, and repetitive/restricted behavior? The hypotheses were:

$H_0$1: ADOS-2 domain scores of socialization, communication, and repetitive/restricted behavior do not differ by age (categorical variable; age 1-4, 5-8, 9-17, 18 and older) and gender.

$H_1$1: ADOS-2 domain scores of socialization, communication, and repetitive/restricted behavior differ by age (categorical variable; age 1-4, 5-8, 9-17, 18 and older) and gender.

A two-way between-groups multivariate analysis of variance was performed to investigate age and gender differences in the different domains measured by the ADOS-2. Three dependent variables were used: communication, socialization and restricted/repetitive behaviors. The independent variables were gender and age. Preliminary assumption testing was conducted to check for normality, linearity, univariate and multivariate outliers, homogeneity of variance-covariance matrices, and multicollinearity, with no serious violations noted. There was a statistically significant difference between the different age groups on the domain scores, dependent variables, $F(9, 171) = 2.64$, $p = .007$; Wilks' Lambda = .73; partial eta squared = .10 (see Table 8).

When the results for the dependent variables were considered separately, the only difference to reach statistical significance, using a Bonferroni adjusted alpha level of .017 (the usual value of .05 was divided by the number of dependent variables), was Socialization Interaction, $F(3, 72) = 3.88$, $p = .012$, partial eta squared = .14. Socialization has an effect on the mean score. An inspection of the mean scores indicated that five-to-eight year-old participants had the highest mean score for the socialization interaction variable ($M = 14.25$, $SD = .99$) in comparison to one-to-four year-old participants ($M = 13.1$, $SD = 0.99$), and 9-17-year-old participants ($M = 13.95$, $SD = .99$). As seen in Table 9, individuals 18 years of age and older had the lowest result average score for the Socialization Interaction domain ($M = 9.96$, $SD = 1.00$). There was not a statistically significant difference between by gender on the dependent variables, $F(9, 171) = 0.97$, $p = .41$; Wilks' Lambda = .96; partial eta squared = .04.

Table 7

Multivariate Tests

Effect		Value	*F*	Hypothesis *df*	Error *df*	*p*	Partial Eta Squared
Intercept	Wilks' Lambda	.07	321.38	3.00	70.00	.00	.93
Age Group	Wilks' Lambda	.73	2.64	9.00	170.51	.007	.10
Gender	Wilks' Lambda	.96	.97	3.00	70.00	.41	.04

Table 8 (cont'd.)

Age Group * Gender	Wilks' Lambda	.84	1.41	9.00	170.51	.19	.06

Table 8

Estimated Marginal Means for the Independent Variables

Dependent Variable	Age Group	*M*	*SE*
Communication (Com-C)	1-4 years	2.15	.24
	5-8 years	1.85	.24
	9-17 years	2.05	.24
	18-older	2.61	.25
Socialization Interaction (Soc-S)	1-4 years	13.10	.99
	5-8 years	14.25	.99
	9-17 years	13.95	.99
	18-older	9.96	1.00
Restricted/Repetitive Behavioral (RRB-R)	1-4 years	3.95	.42
	5-8 years	4.45	.42
	9-17 years	4.75	.42
	18-older	4.51	.42
	<u>Gender</u>		
Communication (Com-C)	Male	2.19	.17
	Female	2.14	.18
Socialization Interaction (Soc-S)	Male	12.89	.69

Table 9 (cont'd.)

	Female	12.74	.71
Restricted/Repetitive Behavioral (RRB-R)	Male	4.75	.29
	Female	4.08	.30

Thus, given the results of there being a main effect for age, the null hypothesis that the ADOS-2 domain scores of socialization, communication, and repetitive/restricted behavior do not differ by age (categorical variable; age 1-4, 5-8, 9-17, 18 and older) and gender was partially rejected. For the null hypotheses for domain scores, age was rejected and gender was accepted.

Research Question 2

Research Question 2 was: Are there age and gender differences in the ADOS-2 total score? The hypotheses were:

$H_0$2: The ADOS-2 total scores do not differ based on gender and age

$H_1$2: The ADOS-2 total scores differ based on gender and age.

A two-way between-groups ANOVA was conducted to explore the impact of age and gender differences on the overall total score on the ADOS-2. As seen in Table 10, the interaction effect between gender and age group was not statistically significant, F (3, 72) = 1.25, p = .30. Furthermore, there were no statistically significant differences or main effect for age (F(3, 72) = 1.28, p = .29) or gender (F(1,72) = .50, p = .48) on the overall mean score (see Table 11).

Table 9

Tests of Between-Subjects Effects

Source	Type III Sum of Squares	*df*	Mean Square	*F*	*p*	Partial Eta Squared
Corrected Model	272.668[a]	7	38.95	1.15	.34	.101
Intercept	30718.219	1	30718.21	908.64	.01	.927
AGEGROUP	129.315	3	43.10	1.28	.29	.050
Gender	17.014	1	17.01	.50	.48	.007
AGEGROUP * Gender	127.055	3	42.35	1.25	.30	.050
Error	2434.082	72	33.80			
Total	33518.000	80				
Corrected Total	2706.750	79				

Note. a. R^2 = .101 (Adjusted R^2 = .013).

Table 10

Descriptive Statistics for Total Score by Age group and Gender

Age Group	Gender	*M*	*SD*	*N*
1-4 years	Male	18.60	5.52	10
	Female	20.70	4.62	10
	Total	19.65	5.07	20
5-8 years	Male	20.80	3.61	10
	Female	20.30	4.76	10

Table 11

	Total	20.55	4.12	20
9-17 years	Male	23.20	5.39	10
	Female	18.30	5.96	10
	Total	20.75	6.08	20
18-older	Male	17.73	8.00	11
	Female	17.33	7.28	9
	Total	17.55	7.49	20
Total	Male	20.02	6.08	41
	Female	19.21	5.65	39
	Total	19.62	5.85	80

Thus, given the lack of a statistically significant main effect for age or gender or an interaction effect, I failed to reject the null hypothesis.

Summary

There is an age difference based on the domains of ASD. The purpose of this study was to examine how the differences in age and gender of ASD, are related to total scores and domain scores of communication, socialization and restricted/repetitive behaviors, measured by the ADOS-2. Archival data from an autistic population was used. There were two independent variables: age (ages 1-4, 5-8, 9-17, and 18+), and gender (male and female). The four dependent variables were three domain scores and total score measured by the ADOS-2. There were two statistical tests used, the MANOVA and 2-way ANOVA. There were two hypotheses and research questions to determined

differences for by age and gender for domain and total scores. The first research question demonstrated significant difference for age groups on the domain scores. Also, there were no differences for genders on the domain scores. The second research question cannot reject the null hypothesis that there were no differences in age groups and genders for total scores. These findings provide essential information on the neurodevelopmental functioning of individuals with ASD, as well as implications for further research on age and gender differences in autism.

Chapter 5: Discussion and Conclusion

The findings of this current study provided vital information with which to generate further research with the ASD population, in order to be able to better serve them. I examined how differences in age and gender were related to total score and domain scores for communication, socialization and restricted/repetitive behavior of ASD, as measured by the ADOS-2. Using the results of this study, I sought to determine if differences in age and gender were related to the neurodevelopmental components of the ADOS-2 scores.

This study was done using a quantitative comparative analysis. A relationship between age and gender and that of domain and total scores was hypothesized. This was a quasi-experiment with random and non-random categorizations of the sample. Two statistical tests were used: MANOVA and 2-way ANOVA. The sample used was from an archival pool of ASD participants administered the ADOS-2. The independent variables were age and gender. Age had four groupings and gender had two. There are four dependent variables, which were the ADOS-2 total score and domain scores for socialization, communication and sensory/motor behaviors).

I investigated two research questions. The first was partially statistically significant. Significant differences between the age groups (IV) for domain scores (DV) were found. For the same question, but different IVs, there were no significant differences or main effects for gender (IV) on domain scores (DV). On the other hand, findings on the second research question showed no significant differences or main effects for both IVs, age groups, and genders for combined total scores (DV).

The statistical tests were further studied to locate significant differences between age groups and find which domain scores most strongly interacted with the various groups. As such, a post hoc test was conducted to identify where differences existed among age groups. The test showed that there was an effect on the mean score for socialization interaction. Further inspection of the mean scores indicated that ages 5-8 had the highest mean score for socialization interaction compared to the other three age groups. However, the 18 and older group had the lowest average score, indicating the lowest interaction level for socialization.

Per the findings, there was alignment with maturation and transition in the 5-7 age group, known as the 5-7 shift. The 5-7 shift is based on middle childhood development, and related to age difference and the social components used in this study (Sameroff & Haith, 1996). Also, it may warrant further investigation based on these findings.

Discussion

Interpretation of Findings

I tested for age and gender differences for the ADOS-2 domain and total scores for an ASD population. The findings indicated that there was a significant difference based on age groups for the ADOS-2 domain scores for the autism population. However, there were no significant differences for gender on ADOS-2 domain scores. In addition, there were no significant differences for age and gender on the ADOS-2 total scores.

Considering age and gender differences added to the complexities of various factors that comprise the autistic spectrum. The findings on age and gender roles in ASD were congruent with various research findings on the topic. With the literature review in Chapter 2, Iboth supported and refuted the impact of age and gender on ASD. Age was

found to be related to the neurodevelopmental components of ASD. There was an age difference in domain scores for ASD, but age and gender did not indicate any differences in the overall total scores. Despite the complexity of various diagnoses on the autistic spectrum, age difference was related to the domain scores of ASD. Daniel and Mandell's (2013) research of 42 peer-reviewed articles, found articles on both sides of this subject.

This current study was consistent with research done by Zielinski et al. (2012) on deficits of neurological functioning in ASD and demonstrated an age difference in the neurodevelopmental components of ASD. This finding is related to the theoretical framework used by Zielinski et al. on the neurological functioning of ASD. Zielinski et al. identified the ICN (SN + DMN) as the structural neurological network involved in the clinical manifestations of ASD (2012). He elaborated that disruption of the neurological systems has an impact on neurodevelopmental systems.

By patterning the current study after Zielinski et al.'s (2012) work on disruptions of neurological structures in the ICN, it clarifies the relationship between neurodevelopmental functioning and behavioral aspects of ASD. Another implication from the current study was the impact of age on development and its effect on neurodevelopmental functioning in ASD. Zielinski et al.'s research found disruptions for younger males only, which was confirmed.

The age group from 5-8 years old was examined. An avenue for further research may be to embed the findings of the current study with the 5-7 shift. The theory of the 5-7 shift was that the transitions during middle childhood development, known as the age of reasoning (Sameroff & Haith, 1996). Development in these years is shaped by cultural

and interpersonal relationship, which mark the child's self-actualizing and acquiring competencies.

Some of the theories on middle childhood development are based on the significant 5-7 shift (Perraudin & Mounoud, 2009). Some of the theorists who explored the 5-7 shift were Freud, Piaget, Vygotsky, and Erickson (Collins, 1984). Freud's middle childhood development was based on the latency period from 6 years to puberty, which was based on skill building around peers. Piaget's theory was partially based on the middle childhood development that included the pre-operational and concrete stages. Piaget developmental stages were based on cognitive development, which shifted from the pre-operational (ages 5-6) egocentric development, to the concrete (ages 7-11) of logical reasoning (Collins, 1984). These theories were indicative of the differences related to age. This is also in accord with the findings on age differences. These changes point to the need for further research on the role of age difference and the 5-7 shift, particularly as they relate to ASD.

In addition to significance attributable to age difference, I found significance for socialization component of ASD as well. This is another implication for further research that corresponded to the findings of the current study involving the domain of socialization and classic developmental theories on social development. Many developmental theories were based on social development (Perraudin & Mounoud, 2009). Although Piaget's and Vygotsky's theories are vastly different, they both emphasize social and constructivist views of development (Fischer & Bullock, 1981). Vygotsky's theory emphasizes social development based on continuous growth. Piaget's was based on four distinct stages. Similar to Piaget's theories on school-aged development,

Erickson's theories on this period were based on various developmental stages (Fisher & Bullock). Erickson's stage for ages 5-12 is based on the industry period that was built on social competency. This is an indication that the social construct of development in that stage could be related to the age difference found in the current study. This connection may be worth exploring in future research.

The current research findings are aligned with the 5-7 shift for both age and socialization. There was significance for age difference for the 5-8 age group, which aligned with the 5-7 shift. In addition to significance for age difference, significance for the socialization component was found. These findings could be further researched concerning age differences, social development, and the 5-7 shift.

There was no gender difference in the neurodevelopmental functioning of individuals with ASD. However, it found age differences without reference to gender. The results of this research went beyond Zielinski et al.'s (2012) work to examine age difference and established a significant difference in males only. They did not examine age difference among the males. Nonetheless, there seems to be an alignment in theories when the two studies are taken together.

In addition, this study's finding on the difference for the 5-8 age group, and Zielinski et al.'s (2012) finding on males, may collectively be useful for treatment given to boys. On the other hand, researchers could utilize their research to explore the implications of females age 5-8 as well.

Another implication of this study may be to investigate the various theories on the 5-7 shift to examine gender difference. Unlike Zielinski et al.'s study on males, many

theorists did not differentiate a gender difference in the 5-7 shift (Collins, 1984). It may be interesting to examine males' performance in comparison to females at 5-7 years old.

This current research did not find significant differences in gender for domain and total ADOS-2 scores for those already diagnosed with autism. However, Daniels and Mandell (2013) found that the incidence of ASD was greater in boys. The findings of this study did not align with their findings in this regard, because no gender difference was shown. Daniels and Mandell also examined some of the factors contributing to gender difference. Some of these were age of testing, masking, and gender stereotyping that boys mainly have ASD. The researchers reported that this bias also caused more boys to be tested for ASD and prevented ASD referrals, testing, diagnosis, and treatment for girls in a timely manner. A recommendation for future research would be to combine the findings of Daniel and Mandell's research with those of this study to explore the impact of boys being tested in comparison to girls.

I sed the coding for the ADOS-2 diagnostic classification to measure the symptoms of ASD represented by the level of severity. The ADOS-2 scores reflect the level of severity for ASD. Levels 0-2 represent minimal to no evidence of ASD (Lord et al., 2012). Levels 3 – 4 are considered low severity or mild ASD; levels 5-7 are moderate severity or moderate ASD; levels 8-and above are high severity or severe ASD.

In this study, I showed that there was a difference in age for domain scores. More specifically there was a statistically significant difference for the 5-8 years old age group and particularly for socialization. The scores were higher for the 5-8 years old age group and were also higher on the socialization domain. The higher the scores, the higher the level of severity of ASD. This indicated that the 5-8 yeatrs old age group was more

severe when compared to the other age groups (ages 1-4, 5-8, 9-17, and 18-older). In addition, the socialization scores were higher when compared to the other domain scores, such as communication and restricted/repetitive behavior. Since the 5-8 years old age group and socialization scores were comparatively higher, it represented more impairment. Therefore, the 5-8 years old age group for socialization as a cluster was more severely impaired than the other categories.

Limitations

The ASD population was randomly selected to include various ethnicities, religions, socio-economic groups, sexual preference, and other differences. This posed a limitation because there were no parameters for any group in the study. There was no identification of the types of group included or excluded from the sample. For example, the sample could have been a mixture of diverse groups, or predominantly one group. As this sample did not specify particular groups, it created a limitation.

Trustworthiness, Validity, and Reliability of Data

The dataset used for the current study was extracted from a large database with the ADOS-2 scores (NDAR/NIH, 2012). These data were housed by the National Institute of Mental Health and collected by the National Database of Autism Research (NIMH-NDAR, 2015). The NIMH data repository was governed by federal regulations concerning information security, best practices, and security standards for data access, submission, and analysis. The procedure used to collect, store, and distribute the dataset was subject to the *Federal Tort Claims Act -28 U.S.C. §§ 2671-2680* (NIMH, 2007), and the *Privacy Act System of Record Notice 09-25-0156* (NDAR/NIH, 2012).

The NIMH-NDAR database has scores from thousands of individuals who took

the ADOS-2 instruments. These data were considered essential for empirical research. The datasets selected for the NIMH-NDAR database undergo a rigorous screening process before being accepted into the database. The ADOS-2 data sets were reported to be valid and reliable according to the NIMH data repository standard set forth in *45 Code of Federal Regulations, Part 46* (NIMH-NDAR, 2015), and given in Appendix D.

Recommendations

Implications of the Study, and Future Research

There were no known studies addressing the relationship of age and gender on the neurodevelopmental functioning of individuals with ASD. There was an age difference in domain scores, which added to the body of knowledge. This information may help researchers distinguish how various age groups were related to ASD. The results of this study were that the age group of 5-8 had the highest socialization interactions and these were statistically significant. This may help researchers further investigate the implications of socializing behaviors for this group.

Given the research results, I suggest further research is required to understand why the 5-8 age group and socialization had higher severity scores than the other age groups and domains. Although this is beyond the scope of this study, further researchers could investigate why the result shows this specific group was more impacted. Is there something happening around this period of testing? Are the other age groups more or less impaired at time of testing? Is the neurodevelopment for socialization during 5-8 years in ASD more at risk? Why are the symptoms of socialization more severe during testing for 5-8 years old? Is severity exhibited more or less for other domains during this period? The implication of this result is that the age period of 5-8 years of age for socialization

demonstrates more impairments. In speculating, the result demonstrated a clinical significance for socialization for those 5-8 years old. From a neurodevelopmental standpoint, the age of reasoning is pivotal for socialization during the 5-8 years of age shift. This could demonstrate a decline in neurodevelopmental components for socialization for the 5-8 years old age group. Perhaps during ASD individuals developmental stage, socialization is more compromised around 5-8 years old. Potentially, the neural structures and functions for socialization is more targeted around 5-8 years old because the result showed that the symptoms were more severe during this phase. Future research could examine why socialization is more impacted during ages 5-8.

The ADOS-2 scores showed a istically statsignificant difference in the socialization symptoms for 5-8 year olds for ASD. The ADOS-2 testing seemed to be soliciting a type of response that's scoring higher for socializing symptoms. The ADOS-2 was more sensitive or biased toward socialization for this age period. The ADOS-2 tool may not be as sensitive in targeting socialization responses for the other age groups or other domains. Therefore, future research could investigate why the ADOS-2 scores are higher for socialization for 5-8 year olds.

I also examined how age and gender difference were related to severity (total scores.) The findings revealed no significant difference for age and gender on the total scores. This is applicable information for researchers speculating on this topic. This may be an applicable topic for researchers to explore why and how age and gender did not differ significantly on the overall scores.

The finding on the difference in severity (total) scores may an implication for researchers to investigate if males are more or less impaired than females and vice-versa. Although the finding did not indicate a significant difference for gender on severity (total) performance, the implication on severity could be further explored to address the level of impairments for gender. Even though the level of impairment was beyond the scope of the current study, it warrants further inspection as it pertains to gender difference.

Autism spectrum disorder is comprised of numerous psychiatric disorders along a continuum (spectrum) classified as the ASD. These disorders along the spectrum are classified by their severity. Because each disorder is classified accordingly by severity, this can create complications in distinguishing between the different disorders. The severity of symptoms of one disorder may not represent the severity for the other. Because the ADOS-2 assesses ASD, severity is standardized. The level of severity is classified as mild, moderate and severe across all disorders. It does not indicate any specificity toward mildness for a specific disorder. This can be a cofounding factor when assessing for severity. Future researchers should take into account that severity for each disorder could be a cofounding factor.

In their research, Rutherford et al. (2016) attested that age was a factor in the manifestation of ASD phenotype due to the delay in testing. They reported that delay in testing could contribute to the ways individuals respond as they age. Although it is beyond the scope of this current research, the theory of age delay could be explored further.

Implications for Social Change

The finding of the current study contributed to ASD research. First, using the results of the study contributed to the knowledge base of ASD by finding a significant difference in age for ASD domains. The findings showed that there was an age difference in domain scores, which relate back to the neurodevelopmental functioning of ASD. This was significant for positive social change. The ASD field benefitted from the finding because researchers can utilize the information on age differences to further explore how and why age contributes to the neurodevelopmental functioning of ASD.

Secondly, a social change contributed by this study was the role of gender in the neurodevelopmental aspects of ASD. Vital information for researchers to explore the role of gender in the neurodevelopmental components of ASD domains was given by this study, as well as further directions for researchers to investigate how and why gender does or does not affect neurodevelopmental functioning in ASD.

Finally, and most importantly, a positive social change this current study contributed to was how the findings directly impact those with ASD. ASD is a prevalent disorder, with 1 in 55 individuals is affected. ASD is also a neurological disorder that has a detrimental effect on our society with no known etiology or universal treatment (ADDM, 2016). The findings of this research may help develop diagnostic tools, programs, and treatments for ASD individuals and families. This study provided information for researchers to further develop and implement practices and policies at various levels of government, as well as for community healthcare providers, hospitals, and schools.

Conclusion

The problem that led to the proposed study was insufficient information demonstrating neurodevelopmental links to ASD. Genetic links may account for only 30-40% of the etiology of autism (Schaefer, 2016), leaving 60-70% of the population with no known cause for their autism.

The CDC (2016) reported that 1 in every 55 children has ASD in 2012. In the absence of a clear etiology of ASD, medical treatments are not effective. This lack of knowledge created the gap in literature that led to this study, which explored how age and gender played a role in the neurodevelopmental functioning of individuals with ASD. ASD is a complex neurological disorder which includes various diagnoses. This current study laid the groundwork to explore neurodevelopmental functioning for individuals on the autistic spectrum relating to severity (total) scores on the ADOS-2.

The research had two research questions and hypotheses. The first question investigated the difference between age and gender and how it was related to ASD domain scores. The second question investigated the relationship between age and gender and the ASD total (severity) scores. For the first question, the findings revealed there was a significant difference in age on domain scores, but differences for gender on domain scores were not significant. Specifically, the socialization domain for the 5-8 years old age group were more impaired when compared to other age groups and domains in ASD.

The second research question failed to find significant differences for age and gender on total (severity) scores. However, findings for the two research questions were both significant in terms of positive social change. They added to the body of knowledge about the role of age and gender in the neurodevelopmental functioning of ASD. They

both had implications for researchers to expand their work on ASD. One implication was that age plays a role in the severity of some aspects of the condition, which may prompt further research on testing individuals earlier. Another is that further research on age-related ASD development, in conjunction with the 5-7 shift, may lead to treatment strategies specific for those ages. As the highest statistical significance occurred during the 5-8 period, it warrants further investigation. The data did not show support for gender differences related to ADOS-2 scores. This calls for further research on why this is the case. Furthermore, researchers may investigate gender-specific treatment in relation to the 5-7 shift. A significant difference during the 5-8 shift was found, but I did not examine how gender plays a role. With the findings of this study, I provided a better understanding of the neurodevelopmental functioning of individuals with ASD. Both findings on age and gender differences provided valuable information to further the development of diagnostic/assessment tools, programs, and treatment for ASD.

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Appendix A: Known Human Carcinogens

1. International Agency for Research on Cancer (IARC).

Carcinogenic to Humans	
● Acetaldehyde (from consuming alcoholic beverages)	● Human papilloma virus (HPV) types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 (infection with) (Note: The HPV types that have been classified as carcinogenic to humans can differ by an order of magnitude in risk for cervical cancer)
● Acid mists, strong inorganic	● Human T-cell lymphotropic virus type I (HTLV-1) (infection with)
● Aflatoxins	● Ionizing radiation (all types)
● Alcoholic beverages	● Iron and steel founding (workplace exposure)
● Aluminum production	● Isopropyl alcohol manufacture using strong acids
● 4-Aminobiphenyl	● Kaposi sarcoma herpesvirus (KSHV)/human herpesvirus 8 (HHV-8) (infection with)
● Areca nut	● Leather dust
● Aristolochic acid (and plants containing it)	● Magenta production
● Arsenic and inorganic arsenic compounds	● Melphalan
● Asbestos (all forms) and mineral substances (such as talc or vermiculite) that contain asbestos	● Methoxsalen (8-methoxypsoralen) plus ultraviolet A radiation
● Auramine production	● 4,4'-Methylenebis(chloroaniline) (MOCA)
● Azathioprine	● Mineral oils, untreated or mildly treated
● Benzene	● MOPP and other combined chemotherapy including alkylating agents
● Benzidine and dyes metabolized to benzidine	● 2-Naphthylamine
● Benzo[a]pyrene	● Neutron radiation

● Beryllium and beryllium compounds	● Nickel compounds
● Betel quid, with or without tobacco	● N'-Nitrosonornicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK)
● Bis(chloromethyl)ether and chloromethyl methyl ether (technical-grade)	● *Opisthorchis viverrini* (liver fluke; infection with)
● Busulfan	● Outdoor air pollution
● 1,3-Butadiene	● Painter (workplace exposure as a)
● Cadmium and cadmium compounds	● 3,4,5,3',4'-Pentachlorobiphenyl (PCB-126)
● Chlorambucil	● 2,3,4,7,8-Pentachlorodibenzofuran
● Chlornaphazine	● Phenacetin (and mixtures containing it)
● Chromium (VI) compounds	● Phosphorus-32, as phosphate
● *Clonorchis sinensis* (infection with)	● Plutonium
● Coal, indoor emissions from household combustion	● Radioiodines, including iodine-131
● Coal gasification	● Radionuclides, alpha-particle-emitting, internally deposited (Note: Specific radionuclides for which there is sufficient evidence for carcinogenicity to humans are also listed individually as Group 1 agents)
● Coal-tar distillation	● Radionuclides, beta-particle-emitting, internally deposited (Note: Specific radionuclides for which there is sufficient evidence for carcinogenicity to humans are also listed individually as Group 1 agents)
● Coal-tar pitch	● Radium-224 and its decay products
● Coke production	● Radium-226 and its decay products
● Cyclophosphamide	● Radium-228 and its decay products
● Cyclosporine	● Radon-222 and its decay products
● Diethylstilbestrol	● Rubber manufacturing industry

● Engine exhaust, diesel	● Salted fish (Chinese-style)
● Epstein-Barr virus (infection with)	● *Schistosoma haematobium* (flatworm; infection with)
● Erionite	● Semustine (methyl-CCNU)
● Estrogen postmenopausal therapy	● Shale oils
● Estrogen-progestogen postmenopausal therapy (combined)	● Silica dust, crystalline, in the form of quartz or cristobalite
● Estrogen-progestogen oral contraceptives (combined) (Note: There is also convincing evidence in humans that these agents confer a protective effect against cancer in the endometrium and ovary)	● Solar radiation
● Ethanol in alcoholic beverages	● Soot (as found in workplace exposure of chimney sweeps)
● Ethylene oxide	● Sulfur mustard
● Etoposide	● Tamoxifen (Note: There is also conclusive evidence that tamoxifen reduces the risk of contralateral breast cancer in breast cancer patients)
● Etoposide in combination with cisplatin and bleomycin	● 2,3,7,8-Tetrachlorodibenzo-para-dioxin
● Fission products, including strontium-90	● Thiotepa
● Formaldehyde	● Thorium-232 and its decay products
● Haematite mining (underground)	● Tobacco, smokeless
● *Helicobacter pylori* (infection with)	● Tobacco smoke, secondhand
● Hepatitis B virus (chronic infection with)	● Tobacco smoking
● Hepatitis C virus (chronic infection with)	● ortho-Toluidine
● Human immunodeficiency virus type 1 (HIV-1) (infection with)	● Treosulfan
● Vinyl chloride	● Ultraviolet (UV) radiation, including UVA, UVB, and UVC rays

• Wood dust	• Ultraviolet-emitting tanning devices
• X-and Gamma-radiation	

2. National Toxicology Program (NT13th Report on Carcinogens

Known to be Human Carcinogens	
Aflatoxins	Dyes metabolized to benzidine
Alcoholic beverage consumption	Erionite
4-Aminobiphenyl	Estrogens, steroidal
Analgesic mixtures containing phenacetin	Ethylene oxide
Aristolochic acids	Formaldehyde
Arsenic and inorganic arsenic compounds	Hepatitis B virus
Asbestos	Hepatitis C virus
Azathioprine	Human papilloma viruses: some genital-mucosal types
Benzene	Melphalan
Benzidine	Methoxsalen with ultraviolet A therapy (PUVA)
Beryllium and beryllium compounds	Mineral oils (untreated and mildly treated)
Bis(chloromethyl) ether and technical-grade chloromethyl methyl ether	Mustard gas
1,3-Butadiene	2-Naphthylamine
1,4-Butanediol dimethylsulfonate (also known as busulfan)	Neutrons
Cadmium and cadmium compounds	Nickel compounds
Chlorambucil	Oral tobacco products
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (MeCCNU)	Radon
Chromium hexavalent compounds	Silica, crystalline (respirable size)
Coal tar pitches	Solar radiation
Coal tars	Soots
Coke oven emissions	Strong inorganic acid mists containing sulfuric acid
Cyclophosphamide	Sunlamps or sunbeds, exposure to
Cyclosporin A	Tamoxifen
Diethylstilbestrol (DES)	2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD); "dioxin"
o-Toluidine	Thiotepa
Vinyl chloride	Thorium dioxide

Ultraviolet (UV) radiation, broad spectrum	Tobacco smoke, environmental
Wood dust	Tobacco, smokeless
X-radiation and gamma radiation	Tobacco smoking

Appendix B: Prevelance of ASD

Autism and Developmental Disability Monitor Rates of ASD 2000-2010.

Identified Prevalence of Autism Spectrum Disorder

ADDM Network 2000-2010

Combining Data from All Sites

Surveillance Year	Birth Year	Number of ADDM Sites Reporting	Prevalence per 1,000 Children (Range)	This is about 1 in X children...
2000	1992	6	6.7 (4.5 – 9.9)	1 in 150
2002	1994	14	6.6 (3.3 – 10.6)	1 in 150
2004	1996	8	8.0 (4.6 – 9.8)	1 in 125
2006	1998	11	9.0 (4.2 – 12.1)	1 in 110
2008	2000	14	11.3 (4.8 – 21.2)	1 in 88
2010	2002	11	14.7 (5.7 – 21.9)	1 in 68

Appendix C: Title

Table C1

Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	*df*	Mean Square	*F*	*p*	Partial Eta Squared
AGEGROUP	Communication (Com-C)	6.10	3	2.03	1.69	.17	.06
	Socialization Interaction (Soc-S)	230.00	3	76.66	3.88	.01	.13
	Restricted/Repetitive Behavioral (RRB-R)	6.77	3	2.25	.65	.58	.02
Gender	Communication (Com-C)	.04	1	.04	.03	.85	.000
	Socialization Interaction (Soc-S)	.46	1	.46	.02	.87	.000
	Restricted/Repetitive Behavioral (RRB-R)	9.07	1	9.07	2.62	.11	.035
AGEGROUP * Gender	Communication (Com-C)	.582	3	.194	.162	.922	.007
	Socialization Interaction (Soc-S)	69.281	3	23.094	1.169	.328	.046
	Restricted/Repetitive Behavioral (RRB-R)	26.099	3	8.700	2.513	.065	.095

Appendix D: NIMH-NDAE Data Repository, Data Use Certificate

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NIMH Data Repositories

Data Use Certification

Last updated: February 28, 2015

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NIMH Data Repositories Data Use Certification

I. Introduction

The National Institute of Mental Health (NIMH) Data Repositories are a group of Federal data repositories based on an informatics platform for research domains related to mental health, initially established as the National Database for Autism Research to support autism-related research. As of June 2014, the system has expanded to include the following repositories:

- National Database for Autism Research (NDAR)—data submission and access
- National Database for Clinical Trials Related to Mental Illness (NDCT)—data submission and access
- Research Domain Criteria Database (RDoCdb)—data submission and access
- NIH Pediatric MRI Repository (PedsMRI)—data access only

This form is for purposes of requesting permission to access data from the NIMH Data Repositories. Recipients seeking access to data from any of the NIMH Data Repositories must submit a Data Use Certification (DUC) certified and co-signed by the Principal Investigator and the designated Institutional Official(s). In order to submit data to the NIMH Data Repositories, the NIMH Data Repositories Data Submission Agreement must be completed, which is a separate document.

The Data Repositories

The National Institutes of Health (NIH) and NIMH have developed a federation of data repositories to store the collection of data from participants in research studies related to mental health, regardless of the source of funding. The extensive information collected by these studies, and subsequently stored in the National Database for Autism Research (NDAR), the NIH Pediatric MRI Repository (PedsMRI), the National Database for Clinical Trials Related to Mental Illness (NDCT), and the Research Domain Criteria Database (RDoCdb) provides a rare and valuable scientific resource. The NIH and NIMH seek to encourage the use of these resources to achieve rapid scientific progress. In order to take full advantage of such resources and maximize their research value, it is important that data be made available, on appropriate terms and conditions, to the largest possible number of qualified investigators in a timely manner.

National Database for Autism Research (NDAR)

The National Database for Autism Research (NDAR) is an NIH-funded research data repository that aims to accelerate progress in autism spectrum disorder (ASD) research through data sharing, data harmonization, and the reporting of research results.

NIH Pediatric MRI Data Repository (PedsMRI)

The goal of the NIH MRI Study of Normal Brain Development and the resulting Pediatric MRI Data Repository (PedsMRI) is to generate data that can help foster a better understanding of normal brain maturation as a basis for understanding atypical brain development associated with a variety of developmental, neurological, and neuropsychiatric disorders affecting children and adults.

National Database for Clinical Trials Related to Mental Illness (NDCT)

NIMH has made data sharing an expectation for all future clinical trials funded by the NIMH (see NOT-MH-14-015). Researchers are expected to submit both positive and negative data and

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results from NIMH-funded clinical trials to the National Database for Clinical Trials Related to Mental Illness (NDCT). NDCT will provide a system to support the submission, sharing and access of relevant data at all levels of biological and behavioral organization and for all data types. At present, data submitted to NDCT will be the result of grants funded through a series of NIMH funding opportunity announcements (FOAs).

Research Domain Criteria Database (RDoCdb)

The Research Domain Criteria (RDoC) initiative aligns research in genetics, neuroscience, and behavioral science to develop a precision-medicine approach for classifying mental illnesses. In contrast to current symptom-based diagnostic systems for mental illnesses, precision medicine integrates many levels of information for each patient to define a precise diagnosis. Data submitted to the RDoC Database (RDoCdb) will include the results of grants funded through a series of NIMH FOAs in support of the RDoC project, as well as relevant data submitted by other interested investigators, regardless of funding source. More information on the RDoC project and related FOAs can be found at .

II. Definitions

For purposes of this agreement, "data" refers to the information which have been collected and recorded from participants in any study, regardless of the source of funding. For human subjects, data include all research and clinical assessments and information obtained via interviews, direct observations, laboratory tasks and procedures, records reviews, genetic and genomic data, neuroimaging data, psychophysiological assessments, data from physical examinations, etc. The following are not included as data: laboratory notebooks, preliminary analyses, drafts of scientific papers, plans for future research, peer review reports, communications with colleagues, or physical objects, such as gels or laboratory specimens.

A "Submitter" is defined as a researcher with a past or current/active grant, contract, or consulting agreement with the NIH, one of its contractors, or any other funding source, who has submitted data to the NIMH Data Repositories, according to the policies laid out in the NIMH Data Repositories Submission Agreement.

The "Recipient" is a researcher at a non-profit or for-profit organization or corporation with an approved Federal Wide Assurance (FWA) from the Department of Health and Human Services Office for Human Research Protections, as well as any collaborating organizational staff listed in NIMH Data Repositories Data Use Certification. The Recipient requests access to study data at his or her sole risk and at no expense to the study or the NIH.

III. Instructions

1. Read the Data Use Certification (DUC).
2. Complete Section VII. Recipient Information and Certification. List all the collaborating investigators at your organization. By submitting an individual's name on the form, you and your Institutional Official affirm that the collaborators have read and agreed to the terms and conditions within the Data Use Certification (DUC). Collaborators at different organizations/institutions must complete separate requests for the data sponsored by their own organization/institution. Coordinated

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A "Submitter" is defined as a researcher with a past or current/active grant, contract, or consulting agreement with the NIH, one of its contractors, or any other funding source, who has submitted data to the NIMH Data Repositories, according to the policies laid out in the NIMH Data Repositories Submission Agreement.

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III. Instructions

1. Read the

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requests by collaborating organizations should all use the same title in their request and each should reference the others in the Research Use Statement.

3. Sign and date the Section VII. Recipient Information and Certification page, and obtain an Institutional Official's signature and date. Only signatures by institutional officials listed as a signing official (SO) in the eRA Commons system will be accepted.
4. Provide a scanned copy of this complete document including the instructions and Data Use Certification pages, with appropriate signatures, to the NIMH Data Repositories within the systems described or email the document to NDAHelp@mail.nih.gov.
5. The appropriate Data Access Committee (DAC) will review the DUC and will decide whether to permit the access based on the expectations outlined in the DUC. In the event that access raises concerns related to privacy and confidentiality, risks to populations or groups, or other concerns, the DAC will consult with other experts as appropriate. Such reviews are generally completed within 10 business days.
6. The DAC(s) will notify NIMH Data Repositories staff if the access request has been approved, and appropriate permissions to the Recipient's account will then be provided. The user will receive a notification of their account update with any modified user name, passwords, or instructions for accessing the appropriate data.
7. Optional: System Training (if request approved): Contact NIMH Data Repositories Staff through NDAHelp@mail.nih.gov to discuss specific training needs the user may have and schedule the training and/or to be directed to the appropriate online tutorials.

IV. Terms and Conditions

I request approval to access data from one or more of the datasets within the NIMH Data Repositories for the purpose of scientific investigation or the planning of clinical research studies as described in the following Data Use Certification (DUC). I, and my collaborating investigators at my institution, agree to the following terms:

1. Research Project/Research Use

These data will be used by Recipient in connection with the "Research Project" generally indicated and described in the Research Use Statement on the DUC. If the Project involves Submitter(s), their names and the work they will perform is also included in the Recipient Information and Certifications section.

2. Non-transferability of Agreement

This DUC is not transferable. If the Recipient changes institutions and wishes to retain access to NIMH Data Repositories, a new DUC in which the new institution acknowledges and agrees to the provisions of the DUC is necessary. If the Recipient changes Institutions and does not complete a new DUC, the Recipient agrees to destroy all copies of NIMH Data Repositories dataset(s) obtained under this DUC, including backup or working copies at the original site.

3. Non-Identification of Subjects

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and privacy of all participants, the Recipient who is granted access to these data is expected to adhere to the specifications of this DUC. Failure to do so could result in denial of further access to data.

Recipient agrees that data will not be used to establish the individual identities of any of the study participants from whom data were obtained and/or contact the individual study participant, except as permitted by law (e.g., in connection with a separately negotiated collaboration with the original research team or the enrollment of the consented subject in the Recipient's study). Recipient agrees to notify the NIH as soon as possible if, upon use of NIMH Data Repositories data, the Recipient discovers identifying information in that data.

4. GUID and Access to Submitted Data

The Global Unique Identifier (GUID) is a computer-generated alphanumeric code that is unique to each research participant. The GUID allows NIMH Data Repositories to link together all submitted information on a single participant, giving researchers access to information even if the data were collected at different locations or through different studies. If Recipients request access to data on individuals for whom they themselves have previously submitted data to NIMH Data Repositories, they may gain access to more data about an individual participant than they themselves collected. Consequently, these research activities may be considered "human subjects research" within the scope of 45 C.F.R. 46. Recipients must comply with the requirements contained in 45 C.F.R. 46, as applicable, which may require that they obtain IRB approval of their Research Project. For more guidance, check with your local IRB and/or the Office for Human Research Protections (OHRP).

5. Data Disclaimers

Recipient acknowledges that the NIH does not and cannot warrant the results that may be obtained by using any data included therein. The NIH disclaims all warranties as to the accuracy of the data in NIMH Data Repositories or the performance or fitness of the data for any particular purpose.

6. Notification to the NIH of Publication

Recipient agrees to promptly notify the NIH via email at NIMHDRHelp@mail.nih.gov as to when and where a publication (or other public disclosure) from the Research Project will appear, whether reporting positive or negative results. The notification will include the title, authors, place of publication, and publication date. Recipient also agrees to create an NIMH Data Repositories Study (http://ndar.nih.gov/access_ndar_study.html) to further define the publication (or other disclosure) and link it to the underlying data.

7. Data Access for Research

Data in the NIMH Data Repositories are eligible for access by qualified researchers, pursuant to the terms set forth in this DUC. Recipients acknowledge that other researchers have access to the data and that downloading, utilization, and duplication of research is a distinct possibility.

Data from ongoing studies which have not yet been made broadly accessible to NIMH Data Repositories account holders may be eligible for restricted "Ongoing Study Access" following coordination and consultation with the Submitter and pursuant to the Additional Standards for Accessing Data While a Study is Ongoing.

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8. No Distribution of Data

Recipient agrees to retain control over data, and further agrees not to transfer data, with or without charge, to any other entity or any individual. Recipient agrees not to sell the data in any form to any entity or individual or to distribute the data to anyone other than his/her research staff who will also agree to the terms within this DUC. This applies to all versions of NDAR data, all versions of PedsMRI data, all versions of NDCT data, and all versions of RDoCdb data.

9. Acknowledgments

Submitters have made a substantial long-term contribution to NDAR, PedsMRI, NDCT, and/or RDoCdb by submitting data to the NIMH Data Repositories. The NIH seeks to encourage appropriate data use and collaborative relationships by outside investigators with the Submitters and to ensure that the contribution of the Submitters is appropriately acknowledged.

Recipient agrees to acknowledge the NIMH Data Repositories informatics platform; the appropriate repository (NDAR, and/or PedsMRI, and/or NDCT, and/or RDoCdb); the relevant data identifier(s) (e.g., a serial number generated via the NIMH Data Repositories Study feature [see http://ndar.nih.gov/access_ndar_study.html or similar feature to be made available on the NDCT and RDoCdb Websites]); and, the Recipient's federal research funding sources in any and all oral and written presentations, disclosures, and publications (including abstracts, as space allows) resulting from any and all analyses of data using the NIMH Data Repositories tools, whether or not Recipient is collaborating with Submitter(s). The oral or written presentation, disclosure, or publication should include the following acknowledgement or other similar language, which includes a disclaimer of NIH endorsement, as appropriate:

NDAR Acknowledgement

Data and/or research tools used in the preparation of this manuscript were obtained from the NIH-supported National Database for Autism Research (NDAR). NDAR is a collaborative informatics system created by the National Institutes of Health to provide a national resource to support and accelerate research in autism. Dataset identifier(s): [NIMH Data Repositories Study identification number or associated Digital Object Identifier (DOI)]. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or of the Submitters submitting original data to NDAR.

Pediatric MRI Acknowledgement

Data used in the preparation of this article were obtained from the NIH Pediatric MRI Data Repository created by the NIH MRI Study of Normal Brain Development. This is a multisite, longitudinal study of typically developing children from ages newborn through young adulthood conducted by the Brain Development Cooperative Group and supported by the National Institute of Child Health and Human Development, the National Institute on Drug Abuse, the National Institute of Mental Health, and the National Institute of Neurological Disorders and Stroke (Contract #s N01-HD02-3343, N01-MH9-0002, and N01-NS-9-2314, -2315, -2316, -2317, -2319 and -2320). A listing of the participating sites and a complete listing of the study investigators can be found

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NDCT Acknowledgement

Data and/or research tools used in the preparation of this manuscript were obtained and analyzed from the controlled access datasets distributed from the NIMH-supported National Database for Clinical Trials (NDCT). NDCT is a collaborative informatics system created by the National Institute of Mental Health to provide a national resource to support and accelerate discovery related to clinical trial research in mental health. Dataset identifier(s): [NIMH Data Repositories Study identification number or associated Digital Object Identifier (DOI)]. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIMH or of the Submitters submitting original data to NDCT.

RDoCdb Acknowledgement

Data and/or research tools used in the preparation of this manuscript were obtained and analyzed from the controlled access datasets distributed from the NIMH-supported Research Domain Criteria Database (RDoCdb). RDoCdb is a collaborative informatics system created by the National Institute of Mental Health to store and share data resulting from grants funded through the Research Domain Criteria (RDoC) project. Dataset identifier(s): [NIMH Data Repositories Study identification number or associated Digital Object Identifier (DOI)]. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or of the Submitters submitting original data to RDoCdb.

If the Research Project involves collaboration with Submitters or NIH staff (as indicated in the DUC), then Recipient will acknowledge Submitters or NIH staff as co-authors, if appropriate, on any presentation, disclosure, or publication.

10. Non-Governmental Endorsement; Liability

Recipient agrees not to claim, infer, or imply endorsement by the United States Government, the Department of Health & Human Services, the National Institute of Health, or the National Institute of Mental Health of the Research Project, the entity, or personnel conducting the Research Project or any resulting commercial product(s). The United States Government assumes no liability except to the extent provided under the Federal Tort Claims Act (28 U.S.C. § 2671-2680).

11. Recipient's Compliance with Institutional Requirements

Recipient acknowledges that access, if provided, is for research that is approved by the Institution, which must be operating under an Office of Human Research Protections-approved Federal-wide Assurance. Furthermore, Recipient agrees to comply with all applicable rules for the protection of human subjects, which may include Department of Health and Human Services regulations at 45 C.F.R. Part 46, and other federal and state laws for the use of this data. Recipient agrees to report promptly to the NIH any unanticipated problems involving risks to subjects or others. This DUC is made in addition to, and does not supersede, any of Recipient's institutional policies or any local, State, and/or Federal laws and regulations that provide additional protections for human subjects.

12. Recipient's Permission to Post Information Publicly

Recipient agrees to permit the NIH to summarize, on the appropriate NIMH Data Repositories web site, the Recipient's research use of data along with the Recipient's name and organizational/institutional affiliation.

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13. Privacy Act Notification

The Recipient agrees that information collected from the Recipient, as part of the DUC, may be made public in part or in whole for tracking and reporting purposes. This Privacy Act Notification is provided pursuant to Public Law 93-579, Privacy Act of 1974, 5 U.S.C. Section 552a. Authority for the collection of the information requested below from the recipient comes from the authorities regarding the establishment of the National Institutes of Health, its general authority to conduct and fund research and to provide training assistance, and its general authority to maintain records in connection with these and its other functions (42 U.S.C. 203, 241, 289l-1 and 44 U.S.C. 3101), and Section 301 and 493 of the Public Health Service Act. These records will be maintained in accordance with the Privacy Act System of Record Notice 09-25-0156 (http://oma.od.nih.gov/public/ms/privacy/pafiles/0156.htm) covering "Records of Participants in Programs and Respondents in Surveys Used to Evaluate Programs of the Public Health Service, HHS/PHS/NIH/OD." The primary uses of this information are to document, track, and monitor and evaluate the use of the NIMH Data Repositories datasets, as well as to notify interested recipients of updates, corrections or other changes to the database.

The Federal Privacy Act protects the confidentiality of some NIH records. The NIH and any sites that are provided access to the datasets will have access to the information collected by the NIH from the Recipient, as part of the DUC for the purposes described above. In addition, the Act allows the release of some information without the Recipient's permission; for example, if it is requested by members of Congress or other authorized individuals. The information requested in this DUC is voluntary, but necessary for obtaining access to data in the NIMH Data Repositories.

14. Security

Recipient acknowledges the expectations set forth by the attached "Information Technology Security Best Practices and Security Standards" for the use and security of data.

15. Annual Update/Research Use Reporting

When requested, Recipient will provide to NIMHDRHelp@mail.nih.gov, as applicable, an annual summary of research accomplishments from using NIMH Data Repositories data in an updated biographical sketch or CV. This annual summary may also be submitted via an NIMH Data Repositories web site link if the function is available. The NIH encourages Recipients who publish manuscripts based on a combination of NIMH Data Repositories data and data collected independent of the NIMH Data Repositories to consider submitting the complete analyzed dataset to the NIMH Data Repositories, if possible.

16. Amendments

Amendments to this DUC must be made in writing and signed by authorized representatives of all parties.

17. Termination

Either party may terminate this DUC, without cause, provided 30 days' written notice to the other party. Recipients agree to immediately report violations of this agreement to the appropriate NIMH Data Repositories DAC. Additionally, the NIH may terminate this agreement with 5 days' written notice if the NIH determines, in its sole discretion, that the Recipient has committed a material breach of this DUC. The NIH may, in its sole discretion, provide Recipient with 30 days' notice to remedy a breach before termination. Closed accounts may be reactivated upon submission of an updated NIMH Data Repositories DUC.

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18. One-Year Term and Access Period

Recipients who are granted permission to access data from any of the NIMH Data Repositories receive an account with permission to access the data from a specified repository that is valid for a period of one year. This DUC will automatically terminate at the end of one year. An account may be renewed upon recertification of a new DUC. Accounts that remain inactive for 12 consecutive months may be closed at the discretion of the NIH.

19. Accurate Representations

Recipient expressly certifies that the contents of any statements made or reflected in this document are truthful and accurate.

V. Information Security Best Practices and Security Standards

The purpose of these Security Best Practices and Security Standards, which are subject to applicable law, are to provide minimum security standards and best practices for individuals who use the NIMH Data Repositories to submit, access, and analyze data. Keeping information from the NIMH Data Repositories secure through these best practices is important. Subject to applicable law, Recipients agree to immediately report breaches of data confidentiality to the NIMH Data Repositories DAC(s).

Security Best Practices

We suggest that you:

- Do not attempt to override technical or management controls to access data for which you have not been expressly authorized.
- Do not use your trusted position and access rights to exploit system controls or access data for any reason other than in the performance of the proposed research.
- Do not allow others to use your account. Each user must obtain and use their own account.
- Ensure that anyone directed to use the system has access to, and is aware of, Information Security Best Practices and Security Standards as well as all existing policies and procedures relevant to the use of the NIMH Data Repositories, including but not limited to, the NDAR Policy at http://ndar.nih.gov/policies.html and 45 C.F.R. Part 46.
- Follow the password policy which includes:
  - Choose passwords of at least seven characters including at least three of the following types of characters: capital letters, lower case letters, numeric characters and other special characters.
  - Change your passwords every six months.
  - Protect your password from access by other individuals—for example, store it electronically in a secure location.
- Notify NIMH Data Repositories staff, as permitted by law, at nimhdrhelp@mail.nih.gov of security incidents, or any incidents of suspected fraud, waste or misuse of NIMH Data Repositories or when access to NIMH Data Repositories is no longer required.

Security Standards

- Protect the data, providing access solely to authorized researchers permitted access to such data by your institution or to others as required by law.
- When you download NIMH Data Repositories data, download the data to a secured computer or

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- For the computers hosting NIMH Data Repositories data, ensure that they have the latest security patches and are running virus protection software.
- Make sure the data are protected from anonymous access over the Internet.
- If you leave your office, close out of data files or lock your computer. Consider the installation of a timed screen saver with password protection.
- Avoid storing data on a laptop or other portable medium. If storing data on such a device, consider encrypting the data.
- When finished using the data, destroy the data or otherwise dispose of it properly, as permitted by law.

VI. Burden Disclosure Statement

Public reporting burden for this collection of information is estimated to vary from 15 min to 1.5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. **An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.** Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0667). Do not return the completed form to this address.

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VII. Recipient Information and Certifications

Date: _____

1. Access Request Type:

Application Type		Data Requested
NEW	RENEWAL	
☑	☐	National Database for Autism Research (NDAR)
☑	☐	Pediatric MRI Data Repository (PedsMRI)
☑	☐	National Database for Clinical Trials (NDCT)
☑	☐	Research Domain Criteria Database (RDoCdb)

2. Lead Recipient:

First Name: Jay Last Name: Greiner

Degree: Ph.D. Academic Position (or Title): Professor

Institution: Walden University Department: Health Psychology Research and E

Street Address: 601 South 80th Street

City: Harrisburg State/Province: Pa Zip/Postal Code: 17111-5310

Country: USA Phone: 717-566-3838 ET FAX: _____

Institutional E-mail Address: jay.greiner@waldenu.edu

Research Project (title): Neurodevelopmental Basis of Autism Spectrum Disorder (ASD) based on Age and Gender.

3. Signatures:

By signing and dating this DUC as part of requesting access to data in the NIMH Data Repositories, my Institutional Officials and I certify that we will abide by the DUC for the use of the NIMH Data Repositories. I further acknowledge that I have shared this document with any research staff who will participate in the use of the NIMH Data Repositories. My Institutional Business Official(s) also acknowledges that they have shared this document with appropriate institutional organizations.

Lead Recipient Signature: Jay K Greiner Date: 5/8/17

Authorized Institutional Business Official (as registered in the NIH eRA Commons: https://commons.era.nih.gov/commons/)

Name: _____

Title: _____

FWA#: _____ Signature: _____ Date: _____

E-mail is the preferred method of submission. Paper submissions should be sent to:
Office of Technology Development and Coordination (OTDC), Program Director

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Project Director/Principal Investigator Contact Information (if different from Recipient listed above)

First Name: _____ Last Name: _____

Degree: _____ Academic Position (or Title): _____

Institution: _____ Department: _____

Street Address: _____

City: _____ State/Province: _____ Zip/Postal Code: _____

Country: _____ Phone: _____ FAX: _____

Institutional E-mail Address: _____

Authorized Representative (Institutional Official)

First Name: _____ Last Name: _____

Degree: _____ Academic Position (or Title): _____

Institution: _____ Department: _____

Street Address: _____

City: _____ State/Province: _____ Zip/Postal Code: _____

Country: _____ Phone: _____ FAX: _____

Institutional E-mail Address: _____

Other Project Information:

1. Are Human Subjects involved? ☑ Yes ☐ No

If YES to Human Subjects

Is the Project Exempt from Federal regulations? ☐ Yes ☑ No

If yes, check appropriate exemption number ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6

If no, is the IRB review pending? ☐ Yes ☐ No

IRB Approval Date: _____

2. Provide a brief description of the Research Project stating the objectives, design, analysis plan and type of data you plan to access.

The purpose of this research is to examine how age and gender differences of autism spectrum disorder (ASD), is related to total scores and domain scores (communication, socialization and restricted/repetitive behaviors), measured by Autistic Diagnostic Observational Schedule-Second Edition (ADOS-2). This research will examine the differences between the age groups, and will also examine how impairments demonstrated by severity are more or less important between the age groups. The study will also examine the differences in severity performance to determine if males are more or less impaired than females and vice-versa. And, this research further explores how gender would address by the domain component scores of the ADOS-2. This is quantitative research (n=80) with independent variables (ages 1-4, 5-8, 9-17, and 18 and older), and gender (males and females). The dependent variables are 3 domain scores and the total scores measured by the ADOS-2. The statistical analyses are the MANOVA and the 2-way ANOVA. These tests will determine the relationship and predictability between age and gender, and the domain and the total scores.

The parameters for the data set are:

1. ADOS-2 scores: total (severity) scores.

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Senior/Key Person Profile (Collaborating Investigator)

First Name: Sursatie Last Name: Chetram
Degree: PhD Candida Academic Position (or Title): Student
Institution: Walden University Department: Psychology
Street Address: 10 Juniper Dr
City: North Haven State/Province: CT Zip/Postal Code: 06473
Country: USA Phone: 203-500-6152 FAX:
Institutional E-mail Address: sursatie.chetram@waldenu.edu
Project Role: Dissertation thesis. Other Project Role Category:

Senior/Key Person Profile (Collaborating Investigator)

First Name: Last Name:
Degree: Academic Position (or Title):
Institution: Department:
Street Address:
City: State/Province: Zip/Postal Code:
Country: Phone: FAX:
Institutional E-mail Address:
Project Role: Other Project Role Category:

Senior/Key Person Profile (Collaborating Investigator)

First Name: Last Name:
Degree: Academic Position (or Title):
Institution: Department:
Street Address:
City: State/Province: Zip/Postal Code:
Country: Phone: FAX:
Institutional E-mail Address:
Project Role: Other Project Role Category:

Senior/Key Person Profile (Collaborating Investigator)

First Name: Last Name:
Degree: Academic Position (or Title):
Institution: Department:
Street Address:
City: State/Province: Zip/Postal Code:
Country: Phone: FAX:

Appendix E: Figures

Figure 1: Neurodevelopment: Events of Brain Neural Maturation