

**SOCIAL FUNCTIONING IN ADULTS WITH AUTISM SPECTRUM DISORDER:
THE ROLE OF BIOLOGICAL STRESS RESPONSE AND PSYCHOSOCIAL STRESS**

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Abstract

This study aimed to improve our understanding of social functioning in autism spectrum disorder (ASD) by: (1) identifying differences in stress among adults with ASD and healthy volunteers; and (2) examining the relationship between stress and social functioning in adults with ASD. This study hypothesized that adults with ASD would experience greater stress than healthy volunteers and that there would be a significant, negative relationship between stress and social functioning in adults with ASD. Data were collected from 40 adults with ASD and 25 healthy volunteers during a single session in the laboratory. Repeated measures of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were taken during a social stress challenge task, while salivary cortisol was collected before and after the task. Measures also assessed psychosocial stress (perceived stress and stressful life events), global functioning, social disability, daily living skills, and social impairment. Analyses examined group differences between adults with ASD and healthy volunteers on biological stress response and psychosocial stress using analysis of variance procedures. The relationship between stress and social functioning was analyzed using hierarchical multiple regression procedures separately for biological stress response and psychosocial stress. This research found that adults with ASD and healthy volunteers exhibit remarkably similar patterns of biological stress response, yet the ASD

group reported more psychosocial stress than healthy volunteers. In addition, findings indicated that psychosocial stress was a pertinent predictor of social disability in adults with ASD, but that biological stress response did not predict social functioning in this group. These results suggest that, while adults with ASD experience greater psychosocial stress than healthy volunteers, they do not differ significantly from healthy volunteers in their biological stress response. In addition, the lived experience of stress may have a greater influence on social disability than biological stress response in this population, although a lack of biological stress response difference between adults with ASD and healthy volunteers may be explained by burnout. Future research should examine interventions that might improve social functioning by helping adults with ASD perceive and cope with stress differently.

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DEDICATION

To Jim and Bridget

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1.0 INTRODUCTION

Autism spectrum disorder (ASD) is a chronic, congenital, neurodevelopmental disorder that is characterized by abnormal or impaired development in social interaction and communication and a restricted repertoire of activity and interests (American Psychiatric Association, 2013). Many Americans had their first introduction to an adult with autism via Dustin Hoffman's character of Raymond Babbitt in the 1988 film *Rain Man*, yet the majority of adults with ASD do not have the savant-like abilities portrayed by Raymond that wowed movie viewers and critics alike (McDougle, 2013). On the contrary, adults with ASD experience categorical and substantial challenges with social functioning that produce remarkably poor social outcomes throughout the life course (Howlin, Moss, Savage, & Rutter, 2013; Howlin, Savage, Moss, Tempier, & Rutter, 2014; Levy & Perry, 2011; Magiati, Tay, & Howlin, 2014; Seltzer, Shattuck, Abbeduto, & Greenberg, 2004; Shattuck, Narendorf, et al., 2012; Vannucchi et al., 2014). Most adults with ASD will never go to college, establish an impressive and meaningful career, have a circle of close friends, get married or commit to a life partner, live independently, or become the individual that their family dreamed they would be before they were diagnosed with autism (Anderson, Liang, & Lord, 2014; Gray et al., 2014; Howlin, 2000; Howlin, Goode, Hutton, & Rutter, 2004; Levy & Perry, 2011; McDougle, 2013; Tobin, Drager, & Richardson, 2014).

Yet, despite poor outcomes for these individuals, the autism research community has done little to develop psychosocial treatments that might help adults with ASD lead happier and more productive lives (Bishop-Fitzpatrick, Minshew, & Eack, 2013). Adults with ASD are similarly unsupported by a service system that is theoretically designed to assist the most vulnerable among us (Shattuck, Roux, et al., 2012). It is because of this that effectively addressing the substantial and varied needs of the growing number of adults with autism is one of the greatest challenges currently facing social workers, service providers, and the autism research community. Going forward, effectively serving this population is an issue that is of paramount importance to the various professional entities that serve the population of adults with ASD, and social workers are well poised to apply the ideologies and practices of the discipline to great effect in this realm.

An estimated 50,000 children with ASD (see Chapter 2 for a detailed description of ASD) will turn 18 this year alone (Shattuck, Narendorf, et al., 2012), and the number of adults with ASD who need effective treatments in order to function well in adulthood will increase rapidly in the coming years (Gerhardt & Lainer, 2011; Shattuck, Narendorf, et al., 2012). Poor social outcomes in terms of education, employment, and the development of social relationships are quite common for this group (Howlin, 2000; Levy & Perry, 2011; Seltzer et al., 2004; Shattuck, Narendorf, et al., 2012), yet there is little understanding of discrete biological or behavioral reasons for these poor social outcomes. This limited understanding of the biological and behavioral underpinnings of positive adult outcomes substantially restricts the development of targeted treatments that effectively serve this large and heterogeneous population and might explain why so few studies of interventions or services for adults with ASD have been published (Bishop-Fitzpatrick et al., 2013; Shattuck, Roux, et al., 2012).

Stress factors heavily into adult life, and its successful management is essential for healthy adjustment. Despite work on themes such as social stress and stress reactivity that indicate that children with ASD may experience different responses to stress in novel social situations than children without autism (Corbett, Mendoza, Abdullah, Wegelin, & Levine, 2006; Corbett, Mendoza, Wegelin, Carmean, & Levine, 2008; Corbett, Schupp, Levine, & Mendoza, 2009; Lanni, Schupp, Simon, & Corbett, 2012; Levine et al., 2011; Spratt et al., 2012), little is known about how adults with ASD experience and react to stress. Adults with ASD are likely to have adverse experiences with and reactions to stress (Brereton & Tonge, 2002), and their responses to stress are probably different from healthy adults (Bishop-Fitzpatrick, Mazefsky, Minshew, & Eack, 2015), but only preliminary evidence exists on stress reactivity and psychosocial stress in this population. Beyond this, scholars examining the role of stress in ASD have not addressed the potential large contribution that stress has to adult outcomes, and, more specifically, social functioning, for people with ASD, which is hypothesized to be central to their adjustment in adulthood (Bishop-Fitzpatrick et al., 2015; Brereton & Tonge, 2002). Without a clear understanding of the impact of stress on adult outcomes in ASD, our ability to address, improve, and enhance treatment for adults with ASD by creating interventions designed to target stress management and improve social functioning will remain limited.

The contribution of this dissertation is to establish knowledge about how adults with ASD respond to stress and how they differ in terms of stress from adults who have not been diagnosed with autism, as well as the impact that stress has on adult outcomes in ASD. The research herein is conducted within the context of an intervention trial of Cognitive Enhancement Therapy (CET) and Enriched Supportive Therapy (EST) for persons with ASD living in the community. This research uses data collected during the course of this intervention

trial and newly collected data on stress and social functioning. These data are analyzed in order to investigate differences in stress between adults with ASD and healthy volunteers and characterize the relationship between stress and social functioning in adults with ASD. Such an investigation is particularly important because it begins to test an underlying mechanism (stress) by which social functioning can be improved in ASD, and therefore may serve to focus treatment development efforts in the future aimed at improving social outcomes in adults with ASD through stress management interventions.

The following is a brief introduction to the significance of social functioning in adults with ASD, as well as an overview of the status of current research with regard to understanding stress in individuals with autism that illustrates the need for further research on the relationship between stress and social functioning. This material will be further examined in Chapter 2.

1.1 RELEVANCE TO SOCIAL WORK

Social work's commitment to social justice through the National Association of Social Workers (NASW) Code of Ethics mandates that social workers advocate for and intervene on behalf of vulnerable individuals and/or groups (NASW, 2008). Because they experience significant and long-term social and functional impairments, individuals with ASD and their families are considered a vulnerable group by the profession (Walsh & Corcoran, 2011). The overrepresentation of families of individuals with disabilities, including ASD, in poverty statistics also qualifies those with ASD and their families as vulnerable persons (Neely-Barnes & Dia, 2008; Parish & Cloud, 2006; Parish, Seltzer, Greenberg, & Floyd, 2004). The overall poor functioning of this vulnerable population and the intersection of individual ability and social

constraints surrounding disability issues in autism justifies social work's role in treatment and service provision (Bean & Krcek, 2012).

The intellectual tradition of social work requires an ecological, biopsychosocial perspective from which to view social problems (Germain, 1978; Gitterman & Germain, 2008). This perspective thus posits that social problems should be viewed through a lens that necessarily takes into account the reciprocal relationships between individuals and their environments (Gitterman & Germain, 2008). It is important to note that, based on the biopsychosocial perspective, biological, psychological, and social contexts all play an important role in shaping the individual (Engel, 1977). Thus, from a social work perspective, social problems cannot be fully understood or addressed without considering biological factors, in addition to social and psychological factors, that might influence the development or manifestation of a social problem. Accordingly, the biopsychosocial perspective must be taken into account within a social work research context when addressing the needs of individuals with autism throughout the life course.

While clinical social workers and social work researchers have much to offer to the development and implementation of treatments and services for individuals with ASD, the social work profession has done a relatively poor job of addressing autism and other developmental disabilities in social work research or education relative to other prominent areas of social work practice such as child welfare, mental health, and poverty (Bean & Krcek, 2012; Walsh & Corcoran, 2011). Yet, despite these oversights in social work research and education, social workers do play a prominent and important role in providing services to people with disabilities (Bean & Krcek, 2012), including ASD (Walsh & Corcoran, 2011). A recent NASW report indicates that approximately 75% of clinical social workers see some clients with developmental disabilities (NASW, 2006). In working with individuals with ASD and their families, social

workers often serve as direct practitioners or provide systems interventions (Walsh & Corcoran, 2011). They also play important roles on inter-disciplinary and interprofessional teams, along with professionals from other allied disciplines (Walsh & Corcoran, 2011).

1.2 THE PROBLEM OF POOR SOCIAL FUNCTIONING IN AUTISM

Poor social functioning is a central diagnostic feature of ASD and has far-reaching effects on multiple domains of adult life for affected individuals. Adults with ASD experience a number of neurobiological and biobehavioral deficits that broadly affect the way that they perceive and receive the social environment (Dawson & Bernier, 2007). In turn, these challenges often lead to pervasive issues with social functioning that create poor social outcomes, including widespread problems in social integration, daily living skills, education, employment, and independent living (Anderson et al., 2014; Gray et al., 2014; Howlin, 2000; Howlin et al., 2004; Levy & Perry, 2011; McDougle, 2013; Tobin et al., 2014).

Social outcomes for adults with ASD have historically been very poor (Eaves & Ho, 1996; Howlin et al., 2004; Levy & Perry, 2011). Prior to 1990, only 25% of adults with ASD were classified as having “good” or “fair” outcomes (Levy & Perry, 2011), defined as being employed or in higher education, living independently, and having developed some social relationships. Current evidence indicates that individuals with ASD still have poor social outcomes in adulthood: very few adults with ASD live independently, get married, go to college or receive vocational training, work in competitive jobs, or develop large social networks, and most individuals with ASD remain dependent on their families or on professional service providers indefinitely (Howlin et al., 2013; Seltzer et al., 2004). In fact, across studies, an

average of 50% to 60% of adults with ASD leave school without vocational credentials or a college degree, and 76% are unable to find work. Additionally, the vast majority live either with parents or in residential placement, 90% to 95% are unable to establish long-term romantic relationships, and many are not able to establish meaningful friendships (Levy & Perry, 2011). The problem of poor social functioning and social outcomes in this population is exacerbated by a lack of research that addresses treatments and accompanying policies that provide services for adults with ASD. Notably, recent systematic reviews found only 13 studies that investigate psychosocial interventions (Bishop-Fitzpatrick et al., 2013) and 23 studies that investigate services (Shattuck, Roux, et al., 2012) for adults with ASD that have been published to date.

The impact of poor social functioning for adults with ASD over the life course combined with the growing population of individuals with ASD (CDC, 2014; Shattuck, Narendorf, et al., 2012) make it imperative to develop the knowledge necessary to design effective interventions that can both ameliorate the adverse impact of these conditions and be implemented on a widespread basis in practice settings. Despite research that has examined the myriad challenges and problems faced by children with ASD and has led to the development of an array of effective treatments that have helped children with ASD substantially (Odom, Boyd, Hall, & Hume, 2010; Odom, Collet-Klingenberg, Rogers, & Hatton, 2010; Ruble, Heflinger, Renfrew, & Saunders, 2005), there remains a lack of research that focuses on the specific needs of adults with ASD (Bishop-Fitzpatrick et al., 2013; Gerhardt & Lainer, 2011; Levy & Perry, 2011; Shattuck, Narendorf, et al., 2012) even though the Interagency Autism Coordinating Committee (IACC) has recently recognized that studying treatments and outcomes in adults is critical (IACC, 2013). Most notably, we know very little about the modifiable factors that predict social functioning in adulthood, or why between 50% and 75% of adults with ASD function poorly in completing

secondary or post-secondary education, maintaining employment, living independently, and sustaining social relationships (Eaves & Ho, 1996; Howlin et al., 2004; Levy & Perry, 2011; Shattuck, Narendorf, et al., 2012). We know even less about how to improve these outcomes through some combination of treatments and services designed to target modifiable predictors that may lead to better social functioning. This research examines potential modifiable predictors of social functioning – biological stress response and psychosocial stress – in order to take the first steps towards developing treatments to help improve social functioning in adults with ASD.

1.3 STRESS RESPONSE IN INDIVIDUALS WITH AUTISM

Adults with ASD face many substantial challenges accomplishing basic tasks associated with daily living (Shattuck, Narendorf, et al., 2012; Smith, Maenner, & Seltzer, 2012; Taylor & Seltzer, 2011) which are further exacerbated by their broad and pervasive difficulties with social interactions (Gillespie-Lynch et al., 2012; Klin et al., 2007; Wing & Gould, 1979). These challenges, coupled with biobehavioral vulnerabilities inherent to ASD (Chamberlain & Herman, 1990; Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Hill, Wagner, Shedlarski, & Sears, 1977; Jansen, Gispens-de Wied, van der Gaag, & van Engeland, 2003), put people with these conditions at increased risk for psychophysiological distress (Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Lanni et al., 2012; Levine et al., 2011; Spratt et al., 2012). Effective management of stress is an essential component of positive social functioning in adulthood (Cohen, Kamarck, & Mermelstein, 1983; Cohen & Williamson, 1988; 1991; Selye, 1956; Williams, 2008). Stress response likely factors heavily into both daily life and long-term outcomes for adults with ASD, as suggested by a growing literature on stress in children with

ASD that indicates that a maladaptive pattern of response to stress starts early and only gets worse over time (Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Lanni et al., 2012; Levine et al., 2011; Spratt et al., 2012). In order to design interventions that might help adults with ASD better manage stress and, as a result, function better in adulthood, we must first understand how adults with ASD perceive and respond to stress and how stress factors into adult outcomes for this population.

A growing, yet nascent, body of research on stress in ASD focuses on characterizing hypothalamic-pituitary-adrenal (HPA) axis and sympathetic-adrenal-medullary (SAM) axis function in order to understand how individuals with ASD respond to stress. HPA axis function and regulation involves a complex network of anatomical structures and neurochemical reactions and is the key biological mechanism for the management of both stress and emotions (Herman & Cullinan, 1997). Moreover, effective stress and emotion regulation have been identified in individuals without autism to be salient predictors of social functioning and adjustment across the life course (Calkins & Marcovitch, 2010; Holahan, Moos, & Schaefer, 1996; Izard, Stark, Trentacosta, & Schultz, 2008; Rossman, Bingham, & Emde, 1997). In individuals with ASD, preliminary research suggests that HPA axis regulation (Corbett et al., 2006; Nir et al., 1995; Richdale & Prior, 1992; Yamazaki, Saito, Okada, Fujieda, & Yamashita, 1975), SAM axis regulation (Goodwin et al., 2006; Groden et al., 2005; Kootz & Cohen, 1981; Lydon et al., 2014; Ming, Julu, Brimacombe, Connor, & Daniels, 2005), and emotion regulation (Mazefsky et al., 2013) may be disturbed, and that stress response may be a key predictor of social functioning in individuals with ASD (Bishop-Fitzpatrick et al., 2015; Mazefsky et al., 2013). This suggests that there may be phenotypic differences in the underlying mechanisms that drive stress and emotion management in individuals with autism and that these differences may be key predictors of

outcomes in this population. However, this research is preliminary, and more work needs to be conducted to understand physiological arousal across the life course and connect variation in stress response patterns to meaningful outcomes.

1.4 OVERVIEW OF STUDY

This study characterizes the nature of stress and how it is related to social functioning in adults with ASD using a combination of psychosocial and biometric measures. All adults with ASD who participated in this research were recruited from an ongoing trial of two psychosocial interventions for adults with ASD – CET and EST – that do not target stress response as a primary focus, but instead involve a stress and emotion management component in either an individual (EST) or group (CET) counseling context. Participants with ASD were assessed during a single session in the laboratory using biometric measures of stress and survey measures of psychosocial stress, global functioning, social impairment, and social disability. In addition, a sample of participants who have not been diagnosed with ASD (hereafter referred to as “healthy volunteers”) were recruited and assessed during a single session in the laboratory using the same survey and biometric measures of stress to identify the degree to which adults with ASD experience discrepant stress reactions from unaffected individuals. Within the context of this study, stress data were examined for both participants with ASD and healthy volunteers in order to assess group differences (**Aim #1**). The relationship between stress and social functioning was then examined for individuals with ASD (**Aim #2**).

1.4.1 Study Aims

This study aims to improve our understanding of the biological and behavioral underpinnings of social functioning by examining stress in adults with ASD. This is accomplished by investigating stress differences between adults with ASD and healthy volunteers and by examining the relationship between stress and social functioning in adults with ASD. Specifically, this study aimed to:

Aim #1: Identify differences in stress among treatment-exposed adults with ASD (n=40) and healthy volunteers (n=25) by examining: (1) cortisol reactivity and cardiovascular reactivity during both a stressor and rest condition in a social stress challenge task; and (2) self-reported psychosocial stress. Data collected during a single session in the laboratory were used to assess differences between treatment-exposed adults with ASD and healthy volunteers measured in terms of cortisol reactivity, cardiovascular reactivity, and psychosocial stress.

Hypothesis 1a: Treatment-exposed adults with ASD will have greater cortisol reactivity than healthy volunteers.

Hypothesis 1b: Treatment exposed adults with ASD will have greater cardiovascular reactivity than healthy volunteers.

Hypothesis 1c: Treatment exposed adults with ASD will have greater psychosocial stress than healthy volunteers.

Aim #2: Examine the relationship between stress and social functioning – including global functioning, social impairment, social disability, and daily living skills – in treatment-exposed adults with ASD (n=40) via the use of multivariate analysis to predict adult outcomes from stress. The relationship between stress (measured in terms of cardiovascular reactivity and cortisol reactivity, as well as psychosocial stress survey measures) and social functioning

(measured as a z-metric composite of global functioning, social impairment, social disability, and daily living skills) in treatment-exposed adults with ASD were examined.

Hypothesis 2a: There will be a significant relationship between cardiovascular reactivity and social functioning such that treatment-exposed adults with ASD who have increased cardiovascular reactivity will also have poorer social functioning.

Hypothesis 2b: There will be a significant relationship between cortisol reactivity and social functioning such that treatment-exposed adults with ASD who have increased cortisol reactivity will also have poorer social functioning.

Hypothesis 2c: There will be a significant relationship between psychosocial stress and social functioning such that treatment-exposed adults with ASD who report greater psychosocial stress will also have poorer social functioning.

2.0 LITERATURE REVIEW

A study designed to investigate the contribution of stress to social functioning in adults with ASD necessarily brings together a diverse body of literature from social work, psychology, psychiatry, and the allied health disciplines. This chapter provides a review of the literature from these disciplines in order to highlight the central issue of social functioning in adults with autism. It also reviews preliminary evidence that identifies stress as a potentially important contributor to social functioning in adulthood in this population. This chapter begins with an overview of the characteristics and prevalence of ASD, with an eye towards the emergence of autism as a lifespan condition. This is followed by an examination of the historical roots and socio-political response to ASD. Third, it proceeds with a detailed review of the social functioning in adults with autism, including a review of the neurobiological basis for poor social functioning in autism. Fourth, this chapter reviews the literature on stress, with a specific focus on the theoretical foundation of stress and coping, measurement of biological stress response and psychosocial stress, and stress in individuals with ASD. Finally, this chapter concludes with an overview of the current study that highlights the importance of both characterizing differences in stress between adults with and without ASD and identifying the link between stress and social functioning in adults with ASD.

2.1 OVERVIEW OF AUTISM SPECTRUM DISORDER

Autism is a complex and disabling neurodevelopmental disorder that poses significant challenges for affected individuals, their families, and the educational and service systems that sustain and support them. Autism is currently conceptualized as a biologically based, developmental disorder that categorically affects development and functioning throughout the life course, and currently has no known cure. Due in large part to shocking reports of the increase in prevalence of ASD, this condition is now recognized as a major public health concern. This section describes ASD as it is currently conceptualized, discusses the increasing prevalence of ASD, and examines its emergence as a lifespan condition.

2.1.1 Characteristics of Autism Spectrum Disorder

Autism is a chronic, congenital, neurological condition characterized by abnormal or impaired development in social interaction and communication and a restricted repertoire of activity and interests. Individuals with autism have a broad range of abilities and may be diagnosed with autistic disorder, Asperger's disorder, or pervasive developmental disorder not otherwise specified (PDD-NOS) based on diagnostic criteria outlined in the revised fourth version of the *Diagnostic and Statistical Manual for Mental Disorders*. In general, people diagnosed with an ASD typically experience difficulty in three main areas: (1) communication; (2) social interaction; and (3) flexibility of thinking and behavior (Wing & Gould, 1979). The extent of the difficulties that individuals with ASD have in these three domains vary within and between individuals. The current diagnostic criteria outlined in the fifth version of the *Diagnostic and Statistical Manual for Mental Disorders* (DSM-V) describe a condition marked by

substantial deficits in social communication and the presence of restricted interests and repetitive behaviors, which are present from early childhood (American Psychiatric Association, 2013). Deficits in social communication and social interaction may be manifested by: deficits in social-emotional reciprocity (the ability to successfully and effectively participate in social interactions); deficits in nonverbal communicative behaviors used for social interactions (the ability to successfully use or interpret nonverbal behavior); or deficits in developing, maintaining, or understanding relationships (the ability to adjust behavior to suit social contexts or make or maintain friends). Restricted, repetitive patterns of behavior, interests, or activities may be manifested by: stereotyped or repetitive motor movements, use of objects, or speech; insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior; highly restricted, fixated interests that are abnormal in intensity or focus (i.e., special interests); and hyper- or hypo-reactivity to sensory input. These symptoms must be present in the early developmental period (typically between 12 and 24 months of age) and must cause clinically significant impairment in social, occupational, or other important areas of current functioning. Symptoms must also not be better explained by an intellectual disability, although ASD and intellectual disability frequently co-occur (American Psychiatric Association, 2013).

The DSM-V conceptualizes ASD on a continuum of functioning and includes newly determined severity levels for ASD that classify affected individuals as requiring very substantial support (Level 3), requiring substantial support (Level 2), or requiring support (Level 1). Individuals requiring very substantial support initiate and respond to very few social interactions (may be nonverbal) and have extreme inflexibility of behavior, great difficulty coping with change, and may have repetitive behaviors (e.g., hand flapping, constant whole body movements, facial picking, head banging) or special interests (e.g., trains, wheels, watches) that substantially

interfere with daily activities. Individuals requiring substantial support may use simple sentences but have very limited interaction with others or markedly odd nonverbal communication. These individuals also have inflexibility of behavior or repetitive behaviors that are relatively obvious to casual observers and interfere with functioning in a variety of contexts. Finally, individuals requiring support are able to engage in social communication but have marked difficulty with social pragmatics and inflexibility of behavior that interferes with functioning in one or more contexts (American Psychiatric Association, 2013). Greater severity of ASD often, but not necessarily, corresponds with the presence of a co-morbid intellectual disability.

2.1.2 Prevalence of Autism Spectrum Disorder

Autism impacts an ever-growing number of individuals, families, and communities in the United States, and each year, 50,000 more children with autism become adults with autism (Shattuck, Roux, et al., 2012), many of whom are affected greatly by poor social functioning. This condition poses a high public health burden both in terms of the \$3.2 million lifetime societal per capita cost that it carries (Ganz, 2007) and the challenges that it poses for the people it affects and the service delivery system that sustains and supports them. Adults with ASD live their lives with a substantial disability that has sweeping effects on multiple domains of adult life. Adults with ASD face significant challenges with social functioning as a result of the biobehavioral vulnerabilities inherent to the disorder, and these challenges create substantial issues with functioning that social workers must begin to address. While individuals with autism often have great abilities and potential, this potential is lost without good treatment designed to target the demonstrable issues that these individuals have with functioning well in society.

The prevalence of ASD continues to grow and thus impacts an increasing number of individuals, families, and communities. The prevalence of ASD is currently estimated to be 1 in 68 children in the United States, an estimate that represents a 123% increase since the Centers for Disease Control and Prevention (CDC) first began to monitor the prevalence of ASD in 2002 (CDC, 2014). Autism affects boys and girls at different rates; there is evidence of greater prevalence in boys than in girls at 1 in 42 versus 1 in 189, respectively (CDC, 2014). It also affects racial groups differently with current estimates of prevalence of 15.8 per 1,000 for European American children, 12.3 per 1,000 for African American children, and 10.8 per 1,000 for Hispanic children (CDC, 2014).

Historically, the incidence of ASD in special education has increased drastically since the 1990s: within the United States special education system, the total reported number of children between the ages of 6 and 21 enrolled under the autism category increased from 22,445 in the 1994-1995 school year, when it was first monitored (Shattuck, 2006), to 443,761 during the 2011-2012 school year (Data Accountability Center, 2012). This constitutes a 1,877%, or nearly 19-fold, increase over a 17-year period. Most research suggests that this increase is due to increased recognition of ASD, particularly at the higher end of the spectrum (Croen, Grether, Hoogstrate, & Selvin, 2002; Hansen, Schendel, & Parner, 2015; King & Bearman, 2009). Social work research has additionally posited that this drastic increase in prevalence can be accounted for by diagnostic substitution, or the idea that the same child who was identified in administrative records as having another disability 10, 15, or 20 years ago is now identified as having ASD because of shifting referral and diagnostic practices (Shattuck, 2006). Prevalence increases are also explained by other factors, including changes in methods of counting children

in special education, increases in awareness in the general public, and the development of specialist services (Shattuck, 2006).

These dramatically increasing prevalence rates have garnered attention in academic research and the popular media, resulting in the mobilization of families, professionals, the federal government, and other stakeholders (Friedman, Warfield, & Parish, 2013). These reports have also spurred research into the causes of and treatment for ASD (Friedman et al., 2013). However, many stakeholders understand that regardless of the discrete reason or set of reasons for this drastic increase in ASD prevalence, the fact remains that more people than ever before are identified with an ASD diagnosis and experience poor social functioning as a result of their condition.

2.1.3 Autism as a Lifespan Condition

Although symptoms of ASD do not typically abate during the lifespan, historically, issues associated with ASD in adulthood have not received the same degree of attention or focus as those issues associated with autism in childhood (Farley & McMahon, 2014). This disparity is problematic because of the growing number of adults with ASD (Shattuck, Roux, et al., 2012), the relative proportion of the life course spent in adulthood (Seltzer et al., 2004), and the per capita cost of autism in adulthood relative to childhood (\$1.9 billion vs. \$1.3 billion; Ganz, 2007). A number of socio-cultural and historical factors have contributed to the increasing importance of lifespan developmental issues in research on and the treatment of ASD. These include the large-scale closing of state-run psychiatric facilities (deinstitutionalization), the corresponding emphasis on greater access to community-based services and living for individuals with developmental disabilities, and educational advocacy and legislation, which

created greater access to inclusive and effective educational services (LeBlanc, Riley, & Goldsmith, 2008). Additionally, the first cohort of individuals systematically diagnosed with ASD in the 1960s has only recently reached older adulthood, thus limiting the pool of individuals with ASD from whom information about life course developmental outcomes can be gleaned (Farley & McMahon, 2014; Seltzer et al., 2004).

The vast majority of studies that characterize the developmental trajectory of ASD symptomatology find that most adults with ASD exhibit a reduction of ASD symptomatology over time (e.g., Billstedt, Gillberg, & Gillberg, 2005; Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008; Farley & McMahon, 2014; Farley et al., 2009; Kobayashi, Murata, & Yoshinaga, 1992; Rumsey, Rapoport, & Sceery, 1985; Shattuck et al., 2007), with improvements in ASD symptoms plateauing in middle adulthood (Smith et al., 2012). However, given the extreme heterogeneity inherent to ASD, it must be noted that while ASD symptoms for many individual improve over the life course, developmental outcomes do vary. More specifically, some individuals with ASD experience either deterioration or marked improvement in symptoms during adolescence (specifically, puberty) or young adulthood (Farley & McMahon, 2014). Deterioration in symptomatology is usually characterized by regression in specific skills or language functioning or by increases in hyperactivity, aggression, destructive behavior, obsessive behavior, or stereotyped behaviors (Billstedt et al., 2005; Kobayashi et al., 1992). Improvement in functioning, or “recovery” from ASD, has been noted in a very small proportion of individuals who eventually acquire enough adaptive skills that they no longer meet diagnostic criteria for ASD and therefore have “optimal outcomes” (Anderson et al., 2014; Cederlund et al., 2008; Szatmari, Bartolucci, Bremner, Bond, & Rich, 1989), although these individuals still retain

subtle impairments that interfere with fully independent functioning and require ongoing supports (Farley & McMahon, 2014).

As discussed in more detail later in this chapter, affected individuals experience the effects of social disability, which is inherent to ASD, throughout the life course. While children with ASD may experience issues with social functioning that affect their ability to do well in school, make friends, and integrate into the community, adults with ASD experience issues with social functioning that affect their ability to fulfill the roles and responsibilities typically expected of adults in the United States. These problems are compounded by the fact that adults have access to fewer community-based supports than do children with ASD.

2.2 SOCIAL POLICY RESPONSE

The social policy response to autism in adulthood in the United States is characterized by a service cliff at age 21, where individuals are jettisoned from the special education system to fend for services on their own with access to few providers, policies, and treatments. Services that support the needs of children with autism are organized relatively cohesively through the United States special education system (Gerhardt & Lainer, 2011; Shattuck, Wagner, Narendorf, Sterzing, & Hensley, 2011). While the service system for school-aged children provides timely, sufficient, and well-coordinated supports, the adult service system often falls short and does not provide appropriate services needed by adults with ASD. In fact, many adults with autism do not receive any services despite having great need. This may be partially attributable to changes in qualification standards between the systems that support children with ASD and the systems that support adults with ASD. Namely, qualifying for adult intellectual and developmental disabilities

services requires both a diagnosis and an assessment of functional impairment while qualifying for the same services in childhood requires only a diagnosis (Shattuck et al., 2011). Relevant policies, and their impact on adults with ASD, are discussed below.

2.2.1 Autism-Specific Legislation

Very little legislation has been designed specifically to meet the needs of individuals with ASD. However, increases in ASD prevalence (CDC, 2014) and advocacy efforts by parents, individuals with ASD, and foundations have led lawmakers to take some action. Two pieces of recent legislation have focused specifically on people with autism. The first, the Advancement in Pediatric Autism Research Act, which was part of the Children's Health Act of 2000, allocated more money for research on autism and established centers around the country dedicated to autism-specific research activity and dissemination of research. The second, the Combating Autism Act of 2006, reauthorized in 2014 as the Autism CARES Act, authorized funding to better the lives of people with autism and their families by way of improved early childhood screening, expanded education, expanded early intervention, and more efficient referral services. Notably, these pieces of legislation make minimal reference to serving the needs of adults with autism, although the 2014 reauthorization of the Combating Autism Act (H.R. 4361) redistributes some funding formerly designated for research regarding children to research on adults with ASD.

Currently, the two social policies that drive service provision for adults with ASD are the Americans with Disabilities Act (ADA) and Medicaid. Generally speaking, the ADA serves as anti-discrimination policy while Medicaid (and Medicaid Home and Community Based Waivers) provides behavioral and physical health services.

2.2.2 The Americans with Disabilities Act

The ADA of 1990, P.L. 101-336, is civil rights legislation that addresses: (1) employment; (2) access to programs, services, and activities; and (3) public accommodations. Most relevant to autism, under provisions of the ADA, the government must provide equal access to programs, services, and activities, including employment and social services, for all citizens regardless of disability, and employers must make reasonable accommodations for employees with mental or behavioral limitations. It is important to note, however, that regulations and relevant case law indicate that employers should not experience “undue hardship” when accommodating individuals with disabilities. Thus, individuals with disabilities are not covered under the ADA if an accommodation that they need in order to perform the essential functions of a job would cause undue burden on the employer’s financial resources or on other personnel.

2.2.3 Medicaid and Medicaid Waivers.

For adults with ASD, Medicaid benefits are determined largely in connection with eligibility for Supplemental Security Income (SSI) (Volkmar & Wiesner, 2009). In order to receive SSI and Medicaid, adults with autism need to meet income requirements and have assets below \$2,000 (Volkmar & Wiesner, 2009). Adults with ASD who qualify for Medicaid health benefits may also qualify for a Medicaid Home and Community Based Service (HCBS) Waiver. These Waivers provide needed supports and services such as case management, personal care and companion services, supported employment, and assistive technology. However, eligibility criteria for Medicaid HCBS Waivers vary by state, and in most states adults with ASD will not

qualify for an HCBS waiver unless they have a co-occurring intellectual disability or substantial functional limitations. Additionally, the central issue with the Medicaid HCBS Waiver program is that these programs are waivers and only provide special permission to be temporarily part of Medicaid. Thus, adults with ASD are not guaranteed permanent access to Medicaid and must receive special permission to be part of Medicaid, and this special permission must be renewed at regular intervals. Furthermore, even if an individual meets the financial, functional, and diagnostic criteria, the Medicaid HCBS Waiver program is not an entitlement program. Once qualified for an HCBS Waiver, most individuals are placed on long waiting lists for services (Braddock et al., 2011).

In order to support successful and fulfilling living that is consistent with individual abilities, and not collective disabilities, many adults with ASD need continued support throughout the life course. However, adults with autism must meet significant financial and diagnostic criteria in order to qualify for services, and even then may not receive access to needed services, such as those under a Medicaid HCBS Waiver program, because of state-level regulations and/or waiting lists that could delay receipt of services for years, or even decades. This is particularly challenging for adults with ASD and without intellectual disabilities who function normally intellectually but socially very poorly (e.g., Howlin et al., 2014; Magiati et al., 2014; Seltzer et al., 2004). These individuals do not qualify for the majority of services available to adults with ASD who also must meet functional limitation and intellectual disability requirements for more intensive services (Shattuck, Roux, et al., 2012; Shattuck et al., 2011). Yet, although these individuals struggle substantially and categorically with social functioning as a hallmark of their condition, they often receive no supports to help counteract the effect of this social disability.

2.3 SOCIAL FUNCTIONING IN ADULTS WITH AUTISM

Autism is a condition with an unclear, yet substantial, biological basis that is probably influenced in some way by both genes and the environment (Harris, 2014). Because of this, much research has focused on an investigation of biological, neurological, molecular, and environmental factors at the exclusion of psychosocial factors. However, the investigation of psychosocial factors has made considerable progress in the past decade, and we now know much more about how adults with autism function socially and what factors may be related to social functioning in this population. What follows is a review of the literature on social functioning in adults with ASD. This section begins with an overview of what is known about the behavioral basis of poor social functioning in adults with autism. It then leads to a discussion of the current state of the evidence on social functioning and its predictors in adults with ASD.

2.3.1 Behavioral and Neurobiological Basis of Poor Social Functioning in Autism

Individuals with ASD experience a number of core social deficits that are behavioral and neurobiological in nature, and these deficits affect social functioning in multiple domains. These core social deficits indicate an underlying problem with social functioning that is diagnostic of ASD and categorically affects functioning across the life course.

Behavioral deficits. According to Dawson and Bernier (2007), patients with ASD differ from age-matched healthy volunteers in five key behavioral domains of social functioning: (1) social orienting; (2) joint attention; (3) face processing; (4) motor imitation; and (5) attention to others' emotions. In terms of social orienting, individuals with ASD are less likely than healthy individuals to orient or preferentially look toward social stimuli, such as hand clapping or a voice

calling their name, shortly after birth (Dawson et al., 2004). Studies of joint attention, or the ability to share awareness or attention with others (Neuhaus, Beauchaine, & Bernier, 2010), indicate that individuals with ASD show very well-documented deficits in initiation, following, and sharing (Dawson et al., 2004). Individuals with ASD also use less holistic face processing strategies and place greater emphasis on specific facial features rather than the whole face, which leads to decreased accuracy and efficiency relative to healthy individuals during face recognition tasks which assess expression, gaze direction, or sex (e.g., Kleinhan et al., 2008; Lahaie et al., 2006). Studies of motor imitation indicate that these individuals experience deficits in spontaneous and prompted imitation of basic hand, facial, and body movements; are less likely to imitate the style with which a motor activity was performed; and do not discriminate between accidental and intentional actions in their imitation (e.g., D'Entremont & Yazbek, 2007; Hobson & Hobson, 2008). Finally, individuals with ASD respond to emotional cues from others differently than do non-affected individuals in that they have difficulty recognizing specific emotions, often do not recognize displays of distress in others, and have trouble understanding what others may be thinking or feeling (Dawson & Bernier, 2007; Swettenham et al., 1998). Taken together, these deficits indicate broad and pervasive challenges with the social-cognitive processes underlying social functioning.

Neurobiological basis of behavioral deficits. Research provides definitive evidence for a neurobiological basis of ASD, yet the specific developmental neurobiology of autism remains speculative and unconfirmed. This is probably indicative of both the overall heterogeneity of autism and the short history of research on its neurobiology (Abrahams & Geschwind, 2008). More specifically, evidence from structural imaging studies suggests that early abnormalities in brain growth either coincide with or predate the emergence of behavioral symptomatology, and

functional imaging studies have provided evidence for the underconnectivity of the neurological systems for social and communicative abilities and core symptoms of ASD (Minshew, Sweeney, Bauman, & Webb, 2005). Consistent across the evidence for the neurobiological basis of ASD is the finding that multiple interconnected brain regions and systems are involved in the presentation of ASD symptomatology (Minshew et al., 2005; Schultz & Robins, 2005).

Data suggest that histological abnormalities, such as increased cerebellar volume (Hardan, Minshew, & Keshavan, 2000; Piven, Bailey, Ranson, & Arndt, 1997; Sparks et al., 2002), reduced hemispheric asymmetry (Herbert et al., 2005; Wan, Marchina, Norton, & Schlaug, 2012), blunted mirror neuron activity (Dapretto et al., 2006; Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2006; Oberman et al., 2005), and underconnectivity throughout the brain (Just, Cherkassky, Keller, Kana, & Minshew, 2007; Just, Cherkassky, Keller, & Minshew, 2004; Just, Keller, Malave, Kana, & Varma, 2012; Kana, Keller, Minshew, & Just, 2007) may be involved. Additionally, structural studies indicate an early acceleration in brain growth that leads to an increase in brain volume in early childhood, as well as increased white matter volume, increased brain weight, and above-average head circumference (Abrahams & Geschwind, 2008; Aylward, Minshew, Field, Sparks, & Singh, 2002; Courchesne, Carper, & Akshoomoff, 2003; Minshew et al., 2005).

Functional studies indicate evidence for underconnectivity in cortical networks that influence social, language, and reasoning function. A number of systems are included in these cortical networks. First, the dorsal medial-frontal cortex and the anterior cingulate, which are indicated in joint attention and social cognition, may be poorly connected in individuals with ASD (Abrahams & Geschwind, 2008; Minshew et al., 2005; Mundy, 2003). Second, the left superior temporal gyrus (Wernicke's area) and the left inferior frontal gyrus (Broca's area),

which are indicated in speech, may show disrupted symmetry patterns in individuals with ASD (De Fossé et al., 2004; Herbert et al., 2002; Just et al., 2004; Schultz & Robins, 2005). Finally, the orbitofrontal/medial temporal circuit, which is involved in theory of mind reasoning (a key aspect of social reasoning), may be disturbed in individuals with ASD (Mundy, 2003; Sabbagh, 2004; Sahyoun, Belliveau, Soulières, Schwartz, & Mody, 2010). These findings have resulted in the emerging perspective that ASD is a disorder of distributed neural systems rather than a focal brain disorder (Minshew et al., 2005), and that the social challenges in the condition are related to underlying deficits in neural processing (Dawson & Bernier, 2007). The previously noted behavioral deficits, along with their neurological basis, are indicative of a disorder in which social functioning is categorically impaired and deficits in social functioning have a strong neurobiological basis. Accordingly, because of the neurobiological basis of these deficits, it is likely that they persist into adulthood despite the developmental nature of the disorder.

2.3.2 Social Functioning in Adults with Autism

Social functioning is usually characterized in the literature in two key ways: (1) in terms of overall ASD symptomatology; and (2) in terms of social outcomes in a number of core domains of adult life. These characterizations are necessarily connected in that the severity of ASD symptomatology greatly affects an individual's ability to function well across many domains of adult life. However, ASD symptomatology and social outcomes should not be conflated because different ASD symptoms (i.e., deficits in communication, deficits in social interaction, and the presence of restricted and repetitive behaviors and interests) have differential effects on the overall level of social outcomes. For instance, an individual with a special interest (restricted and repetitive interest) in a specific type of role-playing game such as Dungeons and

Dragons may not find his or her social functioning inhibited in specialized social contexts and careers where extensive knowledge of and interest in Dungeons and Dragons is valued.

Conversely, an individual who is unable to hold a conversation that follows normative conversation patterns (deficit in communication) may be unable to function well in any situation that requires a conversational exchange. Thus, different ASD symptoms affect social outcomes depending on their relative level of severity, their characterization, and the social context in which they come into play.

Because no clear definition of social functioning is used throughout the ASD literature, this dissertation conceptualizes social functioning in a way that takes into account key domains of ASD symptomatology and performance in social situations, but not social outcomes. These concepts are often incorrectly conflated in the literature but are interconnected such that good overall social functioning can lead to good social outcomes, or vice versa. The conceptualization employed herein more specifically accounts for key aspects of social functioning – including global functioning, social impairment, social disability, and daily living skills – that have been hypothesized in recent research to be central to well-being (Plimley, 2007). This conceptualization takes into account key social skills (i.e., social impairment, social disability) and adaptive functioning (i.e., daily living skills, global functioning) that contribute to overall social functioning. This section discusses the current research on social functioning and outcomes in the key domains of social integration, daily living skills, education and employment, and housing and independent living.

Social integration. Social integration outcomes in adults with ASD can be assessed in terms of the relative extent and quality of dyadic social relationships, including reciprocal friendships and romantic relationships. Overall, the vast majority of adults with ASD fail to

develop reciprocal friendships or romantic relationships (Levy & Perry, 2011), even though qualitative work indicates that they are interested in establishing both friendships (Sperry & Mesibov, 2005) and romantic relationships (Gilmour, Schalomon, & Smith, 2012). A recent study of adults with ASD between the ages of 29 and 64 found that only 9% currently had one or more friend of approximately the same age and only 7% had experienced a close romantic relationship in the past or present (Howlin et al., 2013). Moreover, Howlin and colleagues (2013) also found that 77% of their sample had never had a reciprocal relationship that lasted more than one month, and an additional 17% had some reciprocal relationships that were lacking in emotional intimacy and were short in duration. Another recent study, which utilized a large sample of young adults with ASD from a nationally representative dataset to investigate social participation, found that young adults with ASD were significantly more likely than young adults with other disabilities to never see friends, never be called by friends, never be invited to activities, and be socially isolated (Orsmond, Shattuck, Cooper, Sterzing, & Anderson, 2013).

These recent findings are echoed by historical findings that suggest that only a small minority of adults with ASD develop lasting friendships and relationships (Eaves & Ho, 1996; Szatmari et al., 1989) and that only 5% to 10% of adults with autism have married or established long-term sexual relationships (Eaves & Ho, 1996; Kobayashi et al., 1992). The overarching lack of both quantity and quality of social relationships in adults with ASD indicates that cohesive social integration in the community is rare.

Daily living skills. Limited literature addresses daily living skills in adults with ASD, likely because a questionnaire designed to assess daily living skills in adolescents and adults with ASD, the Waisman Activities of Daily Living Scale (W-ADL), was only recently piloted in the social work literature (Maenner et al., 2013). In the only study to investigate daily living skills in

adults with ASD, Smith, Maenner, and Seltzer (Smith et al., 2012) found that daily living skills improved for individuals with ASD from adolescence through the early 20s but plateaued during the late 20s. Notably, in this sample of adults with ASD, the mean daily living skills score is 20.59 (SD=8.08) on the W-ADL, on which higher scores are better and a score of 34 indicates complete independence. Currently, data are not available on daily living skill improvement trajectories in healthy people, so it is not possible at this time to compare patterns of daily living skills improvement between adults with ASD and healthy volunteers. Thus, adults with ASD likely have very poor daily living skills, but more work is needed in this area to confirm these findings.

Education and employment. One of the major factors underlying poor outcomes for adults with ASD is the inadequacy of educational opportunities and their effect on the attainment of academic or vocational qualifications for later employment and social and economic independence (Levy & Perry, 2011). Across studies, only approximately 50% to 60% of adults with ASD have formal academic or vocational qualifications, including both educational credentials such as a high school diploma or GED or vocational credentials such as certifications or structured work experience (DeMyer et al., 1973; Levy & Perry, 2011; Shattuck, Narendorf, et al., 2012). Beyond this, only a minority of these individuals either attend or successfully complete college (Eaves & Ho, 1996; Kobayashi et al., 1992; Shattuck, Narendorf, et al., 2012; Szatmari et al., 1989).

Associated with issues with educational attainment, adults with ASD have very poor vocational outcomes and experience substantial difficulty maintaining any form of employment, especially competitive employment (Howlin, Alcock, & Burkin, 2005; Howlin et al., 2004; Levy & Perry, 2011; Lotter, 1974; Rumsey et al., 1985). While some adults with ASD do work in

higher-level, independent, and full-time jobs (Lotter, 1974), the majority of the approximately 25% of adults with ASD who are employed work in lower level jobs, often below their qualifications (Levy & Perry, 2011). This is understandable given that many job placement programs that serve this population concentrate on helping people find employment in low-responsibility and low-pay positions (Gerhardt & Lainer, 2011; Howlin et al., 2005).

A recent social work study examined data from a large, nationally representative sample of adults with ASD and compared rates of postsecondary employment and education of youth with ASD to youth with other disabilities (Shattuck, Narendorf, et al., 2012). Results indicated that only 34.7% of youth with ASD attended college and only 55.1% held paid employment at some point during the first six years after high school, rates of participation that are substantially lower than those of youth with other disabilities (Shattuck, Narendorf, et al., 2012). This study also found that higher functional ability and higher family income were associated with a higher probability of participation in postsecondary education or employment.

Housing and independent living. Adults with ASD have access to a number of housing and independent living options yet experience very poor outcomes especially in terms of independent living relative to their level of cognitive functioning. Many adults with ASD remain highly dependent on either their parents, extended families, or other support services well into their late 20s, and this dependency is reflected in data on independent living (Levy & Perry, 2011). Even among the most able adults with ASD with only minor cognitive deficits, 50% to 60% live either with their parents or in structured residential programs in their late 20s (e.g., Cederlund et al., 2008; DeMyer et al., 1973; Eaves & Ho, 1996; Howlin et al., 2004; Kobayashi et al., 1992; Levy & Perry, 2011; Rumsey et al., 1985). These low rates of independent living may harken back to poor overall social functioning and daily or independent living skills.

Unfortunately, no data exists which characterize independent living in less able adults with ASD, though we may assume that rates of full independent living are markedly lower as having an intellectual disability or substantial cognitive deficits is associated with poorer daily living skills (Smith et al., 2012).

2.3.3 Known Contributors to Social Functioning

The vast majority of studies of social functioning in adults with ASD reflect a focus on characterizing adult outcomes rather than identifying prognostic variables. This focus has resulted in a lack of knowledge about predictors of social functioning, especially modifiable predictors, that limits the development of interventions designed to target these predictors, or treatment targets, for this population. Known contributors to social functioning in adults with ASD are primarily characterized in the current research base in terms of childhood factors that predict social functioning in adulthood in individuals with ASD.

Longitudinal studies have identified only two factors that clearly predict adult functioning in children with ASD: (1) an average or above average intelligence quotient (IQ) score; and (2) the ability to communicate in phrases and not just words before the age of 6 (Cederlund et al., 2008; Farley & McMahon, 2014; Farley et al., 2009; Gillespie-Lynch et al., 2012; Howlin et al., 2004; Kobayashi et al., 1992). However, additional cross-sectional research reports that the severity of ASD symptomatology (Rutter, Greenfeld, & Lockyer, 1967), nonverbal problem solving abilities (Szatmari et al., 1989), and ability to engage in joint attention (Gillespie-Lynch et al., 2012) are predictive of adult outcomes.

The most extensively documented childhood predictor of adult outcomes is childhood IQ. Very early, research began to suggest that IQ in childhood was related to eventual adult outcome

(Rutter et al., 1967). An early study found a strong correlation ($r = .60$) between childhood full-scale IQ and adaptive behavior in adults with ASD. In another early study, Kobayashi and colleagues (1992) found in a sample of Japanese adults with ASD that IQ at age six is significantly associated with adult adaptive functioning in both males and females. More recently, Cederlund and colleagues (2008) found in a longitudinal study that childhood verbal IQ was associated with better outcomes in terms of relative functional level in adults with ASD, with individuals with very low verbal IQ scores experiencing very restricted outcomes overall. Similarly, Howlin and colleagues (2004) found that individuals with a childhood performance IQ score of at least 70 experienced markedly better outcomes, with greater independence and functional ability, than individuals with childhood performance IQ scores below 70. Additionally, Gillespie-Lynch and colleagues (2011) found that early childhood (mean age = 3.9 years) IQ predicted adult adaptive behaviors in young adulthood (mean age = 26.6 years). However, it must be noted that in all of these studies, individual outcome is highly variable, and on an individual level, neither verbal nor performance IQ scores in childhood can be considered consistent prognostic indicators of adult outcome.

Additional literature exists that associates childhood language skills, responsiveness to joint attention, nonverbal problem solving abilities, and childhood symptom severity with adult outcomes. A very early study found that individuals who were diagnosed as children with early infantile psychosis who experienced “good” adjustment in adulthood has less severe symptoms as children than those adults who only experienced “fair” adjustment in adulthood (Rutter et al., 1967). Another early study found a strong correlation ($r = .68$) between nonverbal problem-solving ability in childhood and adult adaptive behaviors, as well weaker correlations between facial recognition, motor coordination, and receptive language ability and adult adaptive

behaviors (Szatmari et al., 1989). More recently, Gillespie-Lynch and colleagues (2011) found that early childhood language ability predicted adult adaptive behavior, social functioning, and independence and that early childhood response to joint attention predicted adult social functioning, independence, non-verbal communication, social skills, and ASD symptomatology.

While these studies indicate that childhood factors such as IQ, language and communication ability, symptom severity, and nonverbal problem-solving skills are predictive of outcomes in adulthood in individuals with ASD, this literature is limited in size and scope. Notably, there are few studies that associate childhood factors with adult outcomes, and the existing studies are limitedly powered. Beyond this, these studies focus on factors in children with ASD that predict their outcomes in adulthood. While this is important information for the purpose of early treatment and intervention, these studies exclude factors that might be modifiable treatment targets later in life, thus relegating treatments to intervention in early childhood. This not only excludes a large proportion of the life course and limits intervention options for individuals who are diagnosed later in life; it also implies that outcomes in adulthood can only be improved by treatment in early childhood. Instead, a more balanced approach that takes into consideration the importance of both early intervention and treatment throughout the life course is warranted. As such, it is important to identify predictors of social functioning in adulthood that are modifiable throughout the life course.

2.4 STRESS RESPONSE IN INDIVIDUALS WITH AUTISM

Adults with ASD face many substantial challenges accomplishing basic tasks associated with daily living (Shattuck, Roux, et al., 2012; Smith et al., 2012; Taylor & Seltzer, 2011), which

are further exacerbated by their broad and pervasive difficulties with social interactions (Gillespie-Lynch et al., 2012; Klin et al., 2007; Wing & Gould, 1979). These challenges, coupled with biobehavioral vulnerabilities inherent to ASD (Chamberlain & Herman, 1990; Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Hill et al., 1977; Jansen et al., 2003), put people with these conditions at increased risk for psychophysiological distress (Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Jansen et al., 2003; Lanni et al., 2012; Levine et al., 2011; Spratt et al., 2012). One's ability successfully manage stress is essential to adjustment in adulthood (Cohen et al., 1983; Cohen & Williamson, 1988; Selye, 1956; Williams, 2008), and likely factors heavily into both daily life and long-term outcomes for adults with ASD, as suggested by a growing literature on stress in children with ASD that indicates that these children have differential biobehavioral responses to physiological arousal than children without an ASD diagnosis (Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Lanni et al., 2012; Levine et al., 2011; Spratt et al., 2012). In order to design interventions that might help adults with ASD better manage stress and, as a result, function better in adulthood, we must first understand how adults with ASD perceive and respond to stress and how stress factors into adult outcomes for individuals with ASD.

What follows is a discussion of stress in individuals with ASD. This section begins with a discussion of the theoretical foundation of stress. Then, a discussion of both biological stress response and psychosocial stress is provided. This is followed by a presentation of what is currently known about altered biological stress response and psychosocial stress in individuals with ASD, with specific focus on altered HPA axis and SAM axis activity and emotion regulation in ASD. Finally, the potential of stress as a predictor of social functioning in adults with ASD is reviewed.

2.4.1 Theoretical Foundation of Stress Response

The concept of stress first became part of the public consciousness through the work of Hans Selye (e.g., Selye, 1950; Selye, 1956, 1973) and Richard Lazarus (e.g., Lazarus, 1966, 1974, 1999; Lazarus & Folkman, 1985). While stress was first conceptualized by Selye (1950, 1956) through work in which he observed that exposure to distressing external stimuli produced negative physiological responses in mice, it has since been studied extensively across disciplines (e.g., Caspi et al., 2003; Cohen & Williamson, 1988, 1991; Cohen & Wills, 1985; Kopp, Skrabski, Szekely, Stauder, & Williams, 2007; Williams, 2008; Williams, Barefoot, & Schneiderman, 2003). Stress generally refers to a process via which “environmental demands tax or exceed the adaptive capacity of an organism, resulting in psychological and biological changes that may place persons at risk for disease” (Cohen, Kessler, & Gordon, 1995, p. 3).

Lazarus (Lazarus, 1966, 1974, 1999; Lazarus & Folkman, 1985) has defined stress as a relational concept whereby stress is not viewed as a specific pattern of physiological, behavioral, or subjective reactions but instead as a transaction between individuals and their environment. During this transaction, stress arises when the appraisal made of the demands of a specific situation either tax or exceed an individual’s available resources. Key to this is the concept of cognitive appraisal, which is determined by a number of personal and situational factors. More specifically, each individual appraises situations as stressful or not, and then must deal effectively with situations or experiences that are perceived to be stressful. Accordingly, while stress is a normative and adaptive part of life (Lazarus, 1966; Lazarus & Folkman, 1985; Selye, 1956), the inability to manage stress has been extensively associated with deleterious social, health, and mental health outcomes (e.g., Cohen & Williamson, 1991; Johnson & Sarason, 1978;

Williams, 2008; Williams et al., 2003). It has thus garnered much attention in the research and treatment literature on individuals with and without mental health diagnoses.

Three broad traditions of assessing the role of stress on the development of disease are distinguishable in the literature. First, the environmental tradition concentrates on assessment of stressful life events that are associated with adaptive demands (Cohen, et al., 1995). Second, the psychological tradition focuses on people's perceptions of their abilities to cope with the demands posed by life events (Cohen, et al., 1995). Finally, the biological tradition focuses on the reaction of physiological systems to life events (Cohen, et al., 1995). Broadly speaking, these three traditions of assessing the role of stress on the development of disease come together to create a holistic view of stress by which stressful life events and an individual's perception of the relative stress of those life events come together to create physiological changes that affect the presentation of disease.

2.4.2 Biological Stress Response

Although descriptions of stress vary, almost all conceptualizations of stress hypothesize an integrated biological response pattern both during and after exposure to a stressor (Baum & Grunberg, 1995). This biological response pattern represents an adaptive response to psychological stress and distress whereby biological systems are activated in order to facilitate adaptive, or coping, responses to stress (Schommer, Hellhammer, & Kirschbaum, 2003). The processes that are generally viewed as primarily responsible for these integrated biological response patterns to stress are the combined activation of the sympathetic-adrenal-medullary (SAM) axis and hypothalamic-pituitary-adrenal (HPA) axis (Cohen et al., 1995). The SAM axis is responsible for eliciting the release of catecholamines (epinephrine and norepinephrine) which

result in the elevation of heart rate and blood pressure (Baum & Grunberg, 1995; Krantz & Falconer, 1995) while the HPA axis is responsible for secretion of corticosteroids, including cortisol (Baum & Grunberg, 1995), both during and after exposure to stressors. Individuals' responses to stress are characterized by differential neurobiological responses to specific stressors in terms of both the relative level and reactivity of stress hormones and cardiovascular stress responses during and after stressful situations (Baum & Grunberg, 1995; Cohen et al., 1995; Krantz & Falconer, 1995). These differences are thus often measured by assessing both the level and reactivity of cortisol, heart rate, and blood pressure.

Cortisol (hydrocortisone) is a steroid hormone (glucocorticoid) that is excreted during and after stress in humans. The release of cortisol is triggered by the release of corticosteroids during periods of arousal and distress. Corticosteroids are excreted as part of the systemic arousal of the HPA axis (Baum & Grunberg, 1995). Their excretion is initiated by the release of the corticotropic releasing hormone (CRH) by the hypothalamus in increased quantities during and after exposure to stressors (Taylor, 1988; Timpl et al., 1998). The CRH then stimulates the pituitary gland to produce adrenocorticotrophic hormones (ACTH), which, in turn, triggers the release of corticosteroids from the adrenals (Baum & Grunberg, 1995; Taylor, 1988). This production of corticosteroids by the adrenals is enhanced during stress, and larger quantities of glucocorticoids (cortisol in humans) are then released in bursts into the circulating blood where they are bound rapidly to carriers such as corticosteroid-binding globulin, albumin, and erythrocytes (Kirschbaum & Hellhammer, 2000; Sapolsky, 1996; Sapolsky, Romero, & Munck, 2000). A small amount (2-15%) of cortisol is excreted as "free cortisol" and remains unbound to carriers. This small fraction of excreted and unbound cortisol is responsible for the majority of deleterious effects of cortisol on the body and can only be measured in saliva (Kirschbaum &

Hellhammer, 1989, 1994, 2000). The measurement of salivary free cortisol using saliva samples, rather than other measures of unbound cortisol in urine or blood, also lends itself to benefits, including the ability to assess cortisol without the practical restraints and ethical problems associated with more invasive and costly methods of measuring cortisol excretion, such as blood or urine sampling procedures, which are problematic to measure in vulnerable populations, including individuals with disabilities (Baum & Grunberg, 1995; Kirschbaum & Hellhammer, 1989, 1994, 2000).

2.4.3 Psychosocial Stress

The study of the long-term impact of life events, individual characteristics, and environmental context on human development has spurred a large body of research that focuses on psychosocial risk factors that affect health and well-being throughout the life course. One of these risk factors is stress.

Psychosocial stress has focused on the assessment of stressful life events and their association with adaptive demands. This line of work began in the 1930s with Adolf Meyer, who advocated that physicians should fill out a life chart that included stressful life events as part of the regular examination of patients with physical illnesses (Wolff, Wolf, & Hare, 1950). The basic assumption is that the presence, or lack thereof, of stressful life events, as well as the relative severity of stressful life events experienced by an individual at the same time and over time has a substantial impact on overall well-being and risk for disease (Cohen et al., 1995). Additionally, experiencing a number of stressful life events at the same time or over time can lead to high allostatic load, or wear and tear over time related to chronic stress (Williams, 2008).

The study of psychosocial stress had also focused on individuals' perceptions of their abilities to cope with the demands posed by stressful life events (Cohen, et al., 1995). This model argues that life events are not stressful in and of themselves, but that individuals must appraise, or perceive, life events to be stressful in order for the experience of those life events to create stress. Notably, these perceptions are a product of both the interpretation of a life event and the evaluation of an individual's ability to cope with a life event that is interpreted as stressful (Cohen et al., 1995).

2.4.4 Evidence of Altered Response to Stress in ASD

Parents and caregivers of children with ASD commonly complain about outbursts that are thought to be intense reactions to stressors and are colloquially referred to as “meltdowns” or “tantrums” (Mazefsky et al., 2013). While these “meltdowns” and “tantrums,” and the corresponding intense reactions to stressors that precipitate them, are central to the experience of and discourse surrounding ASD for many affected individuals and their families (Lester & Paulus, 2012), there is a large discrepancy between the perceived centrality of these issues and the extent of empirical evidence surrounding them (Mazefsky et al., 2013). However, in individuals with ASD, preliminary research does suggest that HPA axis regulation (Corbett et al., 2006; Nir et al., 1995; Richdale & Prior, 1992; Yamazaki et al., 1975), SAM axis regulation (Goodwin et al., 2006; Groden et al., 2005; Kootz & Cohen, 1981; Lydon et al., 2014; Ming et al., 2005), and emotion regulation (Mazefsky et al., 2013; Mazefsky & White, 2014; Mazefsky, Pelphrey, & Dahl, 2012; Samson, Huber, & Gross, 2012) may be disturbed in children with autism. There may thus be key differences in the underlying mechanisms that drive stress and emotion management in individuals with ASD.

HPA axis regulation. The study of HPA axis regulation, and more specifically cortisol, in ASD arose from the observation that individuals with ASD adapt poorly to change in their environments (Taylor & Corbett, 2014). Preliminary evidence suggests that HPA axis regulation may be impaired in children with ASD (Corbett et al., 2009; Taylor & Corbett, 2014). More specifically, there is evidence for dysregulation of diurnal rhythm and overall sluggishness of cortisol responsiveness to stressors in children with ASD relative to healthy volunteers (Taylor & Corbett, 2014).

The normal diurnal cycle (diurnal rhythm) of cortisol in typically developing individuals is characterized by a sharp increase in levels during the morning hours followed by a gradual decline throughout the day, and deviation from this pattern is suggestive of HPA axis dysregulation (Smyth et al., 1997). Studies of global dysregulation of the diurnal cycle in autism indicate that few children with ASD exhibit the normal diurnal rhythm such that there is greater variability within and between individuals with ASD and that the slope of cortisol increase is more shallow in individuals with ASD (Corbett et al., 2009; Hill et al., 1977; Hoshino et al., 1984; Yamazaki et al., 1975). However, despite these differences, the overall cortisol output in the system in children with ASD is similar to that of healthy volunteers (Marinović-Ćurin et al., 2008). This indicates that, while overall patterns of cortisol rhythm suggest HPA axis dysregulation in children with ASD, cortisol output in the system throughout the day is similar to that of non-affected individuals.

Studies of specific aspects of the diurnal cycle, including the cortisol awakening response (CAR) and daily decline, add nuance to findings about global diurnal rhythm in ASD. Data on CAR and daily decline in ASD indicates patterns of both failure of the HPA axis to prepare sufficiently for daily stressors and difficulties disengaging from stressful situations (Taylor &

Corbett, 2014). More specifically, findings from studies of CAR, which is a sharp increase of cortisol that occurs approximately 30 minutes after awakening and is thought to represent the reactive capacity of the HPA axis (Schmidt-Reinwald et al., 1999), indicate that children with autism may be less likely to have a CAR (Brosnan, Turner-Cobb, Munro-Naan, & Jessop, 2009; Ćurin et al., 2003; Hamza, Hewedi, & Ismail, 2010), although findings are mixed (Corbett et al., 2006; Corbett et al., 2008; Corbett & Schupp, 2014). Studies of daily decline indicate that afternoon cortisol secretion in children with ASD is probably comparable to that of healthy volunteers (Brosnan et al., 2009; Marinović-Ćurin et al., 2008; Nir et al., 1995; Richdale & Prior, 1992), but that evening levels may be elevated in children with ASD (Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009) after they experience substantial daily challenges. It is important to note that, for both CAR and daily decline, findings are mixed, and definitive conclusions cannot be drawn at this point as these studies are limited by small sample sizes ranging from eight to 50 participants with ASD. These findings do suggest, however, that HPA axis regulation may be disturbed in individuals with ASD.

Given findings that children with autism have similar cortisol output throughout the day but dysregulated diurnal rhythm, reactivity of the HPA axis (specifically cortisol) to stressors in individuals with ASD is of particular importance to understanding overall HPA axis function in this population (Taylor & Corbett, 2014). Early studies of cortisol reactivity in autism focused on cortisol reactivity after injection of the adrenocorticotropic hormone (ACH), which stimulates the adrenal glands to excrete cortisol. These studies have generally found that the HPA axis tends to respond and recover more slowly in children with ASD (Hamza et al., 2010; Hoshino et al., 1984; Marinović-Ćurin et al., 2008). Cortisol reactivity has also been studied in relation to non-social stressors, such as physical activity and medical procedures. When children with ASD are

exposed to non-social stressors, they tend to experience hypo-reactivity in response to physical activity (Jansen et al., 1999; Jansen et al., 2003) and hyper-reactivity in response to medical procedures (Corbett et al., 2008; Corbett et al., 2009; Spratt et al., 2012).

Probably most pertinent to ASD, given that difficulties with social functioning are diagnostic of ASD (American Psychiatric Association, 2013), are stressors that explicitly manipulate the social environment, including stressor paradigms that focus on public speaking, such as the Trier Social Stress Test, or stressor paradigms that focus on more ecologically valid social stressors such as interacting with unfamiliar peers or being separated from one's caregiver (Taylor & Corbett, 2014). Notably, the less ecologically valid public speaking stressor paradigms have found that children with ASD either exhibit no cortisol reactivity (Corbett, Schupp, & Lanni, 2012; Jansen et al., 2003; Lanni et al., 2012; Levine et al., 2011) or less cortisol reactivity than healthy volunteers (Jansen et al., 2003). The stressor paradigms that involve relatively benign social situations, such as interacting with unfamiliar peers or being separated from one's caregiver elicit cortisol hyper-reactivity in children with ASD relative to healthy volunteers (Corbett et al., 2012; Naber et al., 2007; Schupp, Simon, & Corbett, 2013). These findings indicate that children with ASD have differential cortisol reactivity patterns and may experience more stress, leading to more dysregulation, in different types of situations than non-affected individuals. However, there is a pattern of overall sluggishness of cortisol reactivity in children with ASD, even during stressor paradigms in which cortisol hyper-reactivity is experienced (Taylor & Corbett, 2014). Unfortunately, no evidence exists that characterizes the way in which cortisol responds to stressors in adults with ASD, which may be different from children because of the effects of burnout related to allostatic load and the presence of chronic stressors over time (Wong et al., 2012).

SAM axis regulation. In ASD, SAM axis regulation has generally been studied in terms of heart rate, heart rate variability, and blood pressure (Lydon et al., 2014). The literature on SAM axis regulation in autism reveals, like the literature on HPA axis regulation in autism, abnormalities in children with ASD compared to healthy volunteers such that individuals with ASD exhibit different reactivity patterns that are not consistently heightened or blunted. More specifically, children with ASD exhibited greater baseline SAM axis activity (heart rate and blood pressure) (Jansen et al., 2006; Kootz & Cohen, 1981; Ming et al., 2005) and greater SAM axis reactivity (heart rate and heart rate variability) when exposed to a cognitive control (i.e., Stroop) task (Kushki et al., 2013), but lower SAM axis reactivity (heart rate and heart rate variability) when exposed to public speaking stressors (Jansen et al., 2006) or benign social stressors like unstructured time or changes in staff (Goodwin et al., 2006) compared to healthy volunteers. Additionally, children with ASD and a co-morbid anxiety disorder exhibit patterns of blunted SAM axis response to a public speaking task (Hollocks, Howlin, Papadopoulos, Khondoker, & Simonoff, 2014). These findings suggest an overall pattern of dysregulation in SAM axis function, with children with ASD exhibiting overall heightened SAM axis activity, yet hyper-responsiveness and hypo-responsiveness of the SAM axis to different stressor tasks. However, the research to date does not indicate whether adults with ASD differ from healthy volunteers in terms of SAM axis activity or whether SAM axis reactivity is associated with social functioning in adults with ASD.

Emotion regulation. Emotion regulation refers to either the automatic or intentional modification of one's emotions in a way that promotes adaptive behavior, while emotion dysregulation refers to the inability to modify one's emotions in an adaptive manner (Gross, 1998; Gross & Thompson, 2007). Successful emotion regulation is central to the management of

stressful experiences and influences stress response through a process by which individuals experience situations and events as stressful or not based on their emotion regulation capacity (Thompson, 1994). Individuals with ASD have generally poor emotional insight (Hill, Berthoz, & Frith, 2004; Mazefsky et al., 2013) and self-monitoring abilities (Beer, John, Scabini, & Knight, 2006; Mazefsky et al., 2013) and may be substantially less able to understand the expressed emotions of others (Baron-Cohen, 1997; Baron-Cohen, Leslie, & Frith, 1985; Eack, Mazefsky, & Minshew, 2014). The presence of poor emotion regulation in individuals with ASD are probably intrinsic to ASD (Mazefsky et al., 2013; Mazefsky & White, 2014), but may be explained by psychiatric comorbidities (Mazefsky et al., 2013).

A number of characteristics of ASD may contribute to issues with emotion regulation in affected individuals, including: cognitive rigidity; lower inhibition; poor problem solving and abstract reasoning abilities; difficulty reading social and emotional cues; sensitivity to change in the environment; and aforementioned heightened physiological arousal (Mazefsky & White, 2014). Individuals with ASD report higher levels of negative emotions, but similar levels of positive emotions compared to healthy volunteers (Samson et al., 2012). They also have a harder time identifying and describing their emotions (Samson et al., 2012) and use fewer emotional self-regulation strategies (Jahromi, Bryce, & Swanson, 2013; Samson et al., 2012) than healthy volunteers. Research suggests that poor emotion regulation in these individuals may be related to more behavioral disturbances, such as tantrums, meltdowns, aggression, and self-injurious behavior (Mazefsky & White, 2014). These issues with emotion regulation in this population may also exacerbate problems with interaction, communication, and social problem solving (Laurent & Rubin, 2004) and lead to problems with overall social functioning.

Summary of evidence of altered stress reactivity in ASD. Individuals with ASD

experience poor HPA axis regulation and hyperarousal (Taylor & Corbett, 2014), SAM axis dysregulation (Lydon et al., 2014), and issues with emotion regulation (Laurent & Rubin, 2004; Mazefsky et al., 2013; Mazefsky & White, 2014; Samson et al., 2012). While these findings paint an overall picture of dysregulation in the systems that support the biological and emotional responses to stressors, no clear picture emerges of hypo- or hyper-arousal across all systems. Instead, it appears as though individuals with ASD experience generalized dysregulation in these systems, leading to an overall atypical response to stress. Notably, individuals with ASD may experience greater reactivity during relatively benign social situations, which may differentiate them substantially from healthy volunteers. It is likely that poor HPA axis and SAM axis regulation precipitate the appraisal of situations as stressful, and that the appraisal of situations as stressful leads to poorer reactions to stressful situations given that individuals with ASD have a difficult time regulating their emotions. Thus, physiological dysregulation may precipitate issues with emotion regulation such that individuals experience dysregulated responses to stressors, appraise situations as stressful, and then are unable to regulate their emotions surrounding these situations. These issues may be more apparent in relatively benign social situations, leading to an overall pattern of physiological dysregulation that is pronounced during interactions that would not be stressful for unaffected individuals.

While the literature to date has identified a general pattern of physiological dysregulation in children with ASD, it is unclear whether adults with ASD also experience similar physiological dysregulation patterns and if adults with ASD actually experience life to be more stressful than healthy volunteers. In addition, no research to date has examined whether physiological dysregulation predicts social functioning in adults with ASD, although some very

preliminary research has identified perceived and interviewer-observed stress as a potential predictor of social functioning in this population.

2.4.5 Stress as a Predictor of Social Outcomes in Autism

The literature discussed herein indicates that individuals with ASD respond differently to stress than healthy volunteers and have dysregulated psychophysiological reactions to stress. While the literature on stress and stress reactivity in individuals with ASD focuses almost solely on children (Levine et al., 2011; Spratt et al., 2012), it is likely that adults with ASD also experience heightened psychosocial distress and biological stress in social situations. Accordingly, when an adult with ASD experiences stressful life events, his or her appraisal of the relative stress of those life events combines with the event itself to create physiological changes that result from stress.

A great deal of research has examined the impact of life stressors, and the successful management of these life stressors, on social functioning. Indeed, an abundance of evidence suggests that individual differences in management of stress and emotion play a central role in predicting overall social functioning (Eisenberg, Fabes, Guthrie, & Reiser, 2000; Kessler, Price, & Wortman, 1985). Within those not affected by ASD, the literature generally suggests that individuals who can better handle psychosocial distress and can modulate the experience of emotional or physiological arousal better are more likely to behave in socially appropriate ways and function well within the context of social relationships and interactions (Eisenberg & Fabes, 1992; Kessler et al., 1985; Pulkkinen, 1982). Individuals who are able to better regulate their response to distress are also more likely to not experience psychopathology (Kessler et al., 1985). However, the magnitude of the relationship between stress and social functioning is

greatly influenced by context such that an individual's perception of life events as stressful is dependent upon that individual's perception of their ability to handle the stressor based on their current emotional, financial, and social resources. The relationship between stress and social functioning within individuals is also dependent upon how well an individual functions socially, leading to a potentially reciprocal and cumulative relationship between stress and social functioning such that the better one functions socially, the less likely they are to perceive life stressors as stressful, leading to better overall social functioning in the long run (Eisenberg et al., 2000; Kessler et al., 1985). It is thus likely that poorer social functioning leads to heightened distress, although, the prediction of social functioning by stress response (and not the prediction of stress response by social functioning) generally holds across healthy populations (Eisenberg et al., 2000).

Preliminary evidence suggests that stress may be a salient predictor of social functioning in individuals with ASD. A recent, though very preliminary, study examined the relationship between perceived and interviewer-observed stress and social functioning in adults with autism and healthy volunteers (Bishop-Fitzpatrick et al., 2015). In this study, baseline, semi-structured interview data were used to assess differences in perceived and interviewer-observed stress between adults with ASD and healthy volunteers and to assess the relationship between stress response and social functioning in adults with ASD. Findings indicated that adults with ASD experienced greater perceived and interviewer-observed stress than did healthy volunteers and that greater stress was significantly related to poorer social functioning in adults with ASD but not in healthy volunteers.

However, these findings are undermined by a number of methodological limitations. Namely, this study utilized limited and imprecise measures of stress and social functioning (the

Brief Psychiatric Rating Scale and Global Assessment Scale, respectively) that were chosen opportunistically from previously collected clinical trial data. This study also did not include any biological measures of stress response, therefore making it difficult to distinguish between stress response and anxiety. Nonetheless, these preliminary findings suggest that adults with ASD may differ from healthy volunteers in terms of perceived and interviewer-observed stress, and that perceived and interviewer-observed stress may be significantly associated with social functioning. However, these findings warrant the investigation of the relationship between stress and social functioning in adults with ASD using better instrumentation and a combination of psychosocial and biological measures of stress.

2.5 PROPOSED STUDY AND HYPOTHESES

This literature review reveals a number of areas where improved understanding is warranted. The literature discussed herein indicates that adults with ASD experience marked challenges with social functioning that are both diagnostic of ASD and persistent across the life course (Howlin et al., 2004; Howlin et al., 2013; Seltzer et al., 2004; Shattuck & Roux, 2014). In addition to issues with social functioning, individuals with ASD also experience challenges with HPA axis and SAM axis dysregulation (Lydon et al., 2014; Taylor & Corbett, 2014), which are probably tied to issues with emotion regulation (Mazefsky et al., 2013; Mazefsky & White, 2014). These challenges may be particularly pertinent to the management of stress in ASD, which is hypothesized to be a significant issue for most affected individuals (Bishop-Fitzpatrick et al., 2015; Lydon et al., 2014; Taylor & Corbett, 2014). However, we know relatively little about biological stress response and psychosocial stress in adults with ASD. We also have

limited understanding of the relationship between stress and social functioning in ASD (Bishop-Fitzpatrick et al., 2015). It is important to investigate this using a combination of biometric and psychosocial measures in order to paint a holistic picture of this phenomenon.

It follows that a study of stress in adults with ASD is necessary in order to address these gaps in the literature. Thus, this study examines the relationship between stress and social outcomes in adults with ASD using a combination of psychosocial and biometric measures. Within the context of this study, stress data were examined for both participants with ASD and healthy volunteers in order to assess group differences (**Aim #1**). Then, the relationship between stress and social functioning were then examined for individuals with ASD (**Aim #2**).

2.5.1 Aims and Hypotheses

This study aims to improve our understanding of the biological and behavioral underpinnings of social functioning by examining stress in adults with ASD. This goal is accomplished by investigating biological stress response and psychosocial stress differences between adults with ASD and healthy volunteers and by examining the relationship between stress and social functioning in adults with ASD. Specifically, this study aimed to:

Aim #1: Identify differences in stress among treatment-exposed adults with ASD (n=40) and healthy volunteers (n=25) by examining: (1) cortisol reactivity and cardiovascular reactivity during both a stressor and rest condition in a social stress challenge task; and (2) self-reported psychosocial stress. Data collected during a single session in the laboratory were used to assess differences between treatment-exposed adults with ASD and healthy volunteers measured in terms of cortisol reactivity, cardiovascular reactivity, and psychosocial stress.

Hypothesis 1a: Treatment-exposed adults with ASD will have greater cortisol reactivity than healthy volunteers.

Hypothesis 1b: Treatment exposed adults with ASD will have greater cardiovascular reactivity than healthy volunteers.

Hypothesis 1c: Treatment exposed adults with ASD will have greater psychosocial stress than healthy volunteers.

Aim #2: Examine the relationship between stress and social functioning – including global functioning, social impairment, social disability, and daily living skills – in treatment-exposed adults with ASD (n=40) via the use of multivariate analysis to predict adult outcomes from stress. The relationship between stress (measured in terms of cardiovascular reactivity and cortisol reactivity, as well as psychosocial stress survey measures) and social functioning (measured as a z-metric composite of global functioning, social impairment, social disability, and daily living skills) in treatment-exposed adults with ASD was examined.

Hypothesis 2a: There will be a significant relationship between cardiovascular reactivity and social functioning such that treatment-exposed adults with ASD who have increased cardiovascular reactivity will also have poorer social functioning.

Hypothesis 2b: There will be a significant relationship between cortisol reactivity and social functioning such that treatment-exposed adults with ASD who have increased cortisol reactivity will also have poorer social functioning.

Hypothesis 2c: There will be a significant relationship between psychosocial stress and social functioning such that treatment-exposed adults with ASD who report greater psychosocial stress will also have poorer social functioning.

3.0 RESEARCH DESIGN AND METHODOLOGY

This research makes use of a combination of secondary data, routinely collected during the course of an ongoing intervention trial of CET and EST for adults with ASD, and primary data, newly collected for the purpose of this dissertation from participants enrolled in the ongoing intervention trial of CET and EST and a comparison group of healthy volunteers. This combination of secondary and primary data was analyzed to answer several questions concerning the significance of stress response in social functioning in adults with ASD. Specifically, these data were used to examine differences in biological stress response and psychosocial stress in adults with ASD and healthy volunteers. These data were also used to engage in an investigation of the relationship between biological stress response and psychosocial stress and social functioning in adults with ASD, while accounting for shared variance with demographic confounders. This section describes the design, procedures, participants, and measurement techniques, as well as the analytic techniques, used for addressing the aims and evaluating the hypotheses above.

3.1 STUDY DESIGN

This research explored the role of stress in social functioning in adults with ASD by comparing both biological stress response and psychosocial stress in adults with ASD and

healthy volunteers and by exploring the relationship between biological stress response and psychosocial stress and social functioning in adults with ASD using a combination of psychosocial and biometric measures. All adults with ASD who participated in this research were recruited from an ongoing trial of two psychosocial interventions for adults with ASD – CET and EST – that do not target stress response as a primary focus, but instead involve a stress and emotion management component in either an individual (EST) or group (CET) counseling context. These interventions are hypothesized to affect stress in some way, but it is not expected that either of these treatments alone will normalize stress in this population because current knowledge suggests the possibility that the stress reaction of people with autism is so different from normal that even after treatment it is possible that people with ASD will still be quite different from normal.

Participants enrolled in this clinical trial of CET and EST were assessed during a single session in the laboratory using biometric and survey measures of stress, and survey measures of global functioning, social impairment, social disability, and daily living skills. Because this clinical trial was ongoing, participants varied in their treatment exposure at the time of their assessment. In addition, a sample of healthy volunteers were recruited and assessed during a single session in the laboratory using biometric and survey measures of stress to identify the degree to which adults with ASD experienced stress reactions discrepant from unaffected individuals. Within the context of this study, biological stress response and psychosocial stress data were examined for both participants with ASD and healthy volunteers in order to assess group differences (**Aim #1**). Then, the relationship between stress response and social functioning was examined for individuals with ASD (**Aim #2**).

3.2 PARTICIPANTS

In order to address the aims, research questions, and hypotheses delineated above, this study examined data on stress and social functioning collected from both treatment-exposed adults with ASD and healthy volunteers. Forty participants with ASD were recruited from an active clinical trial of CET and EST. Eligibility criteria for this trial included meeting expert clinical opinion and research criteria for ASD using the Autism Diagnostic Observation Schedule (Lord et al., 2000) or criteria for ASD on the Autism Diagnostic Interview-R (Lord, Rutter, & Lecouteur, 1994), being age 16-55, having an IQ > 80 as assessed by the Wechsler Abbreviated Scale of Intelligence (Wechsler, 2008), not abusing substances in 3 months prior to enrollment, not exhibiting substantial and negatively impactful behavior problems, and having significant cognitive and social disability that warranted treatment (Hogarty, Flesher, Ulrich, & et al., 2004). This study utilized slightly different age inclusion criteria than the clinical trial of CET and EST and thus included only adult participants between the ages of 18 and 55. Participants younger than 18 years were excluded from this research, consistent with espoused aims to address the needs of adults with ASD. Additionally, participants older than 55 years were excluded in order to avoid potential confounding issues with morbidity as individuals with developmental disabilities age (Sutherland, Couch, & Iacono, 2002). A complete description of participants with ASD is provided in Chapter 4.

An additional cohort of 25 healthy volunteers matched for age, gender, and race were recruited. These participants were between the ages of 18 and 55, had no current psychiatric disability, as confirmed through the Structured Clinical Interview for the DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 2002) and had no history of cardiovascular disease. Participants who served as healthy volunteers were recruited through a database of participants who had

previously served as healthy volunteers in related autism and schizophrenia studies. Because data were collected during a single study visit, there was no attrition. A complete description of healthy volunteers is provided in Chapter 4.

All data and information collected for this study were treated confidentially, and complied with the policies and procedures governing research with human subjects set forth by the University of Pittsburgh Institutional Review Board (IRB). Psychiatric and medical records evaluated and obtained for screening or recruitment purposes were subject to the standard confidentiality procedures of Western Psychiatric Institute and Clinic, Pittsburgh, PA. All participants were required to provide written, informed consent prior to study participation.

3.3 INTERVENTIONS

3.3.1 Cognitive Enhancement Therapy

CET (Hogarty & Greenwald, 2006) is a unique, experiential, developmental approach to the remediation of neurocognitive and social-cognitive deficits in autism and schizophrenia. The CET program integrates computer-based neurocognitive training exercises designed to improve attention, memory, and problem-solving skills with a social-cognitive group curriculum based on the developmental principle of secondary socialization, or the idea that individuals can learn implicit adult social norms through the process of context appraisal and perspective taking. The CET program thus incorporates, through weekly sessions over an 18-month period, a neurocognitive training program that involves 60 hours of training in cognitive exercises and a 45-session social-cognitive group that focuses on the social-cognitive skills that underlie

effective social interaction. The social-cognitive group includes psychoeducation and social-cognitive training, including information and sessions on stress management. Preliminary evidence of the efficacy of CET in adults with ASD has indicated that CET was highly effective in a small sample of adults with ASD ($n = 14$) at improving neurocognitive ($d = 1.40$) and social-cognitive ($d = 1.36$ to 2.39) functioning and that CET produces long-lasting (18 months) improvements in overall social functioning (Eack et al., 2013).

3.3.2 Enriched Supportive Therapy

Enriched Supportive Therapy (EST) consists of components from the basic and intermediate phases of Personal Therapy (Hogarty, 2002). Personal Therapy, designed for individuals with schizophrenia but adapted in part for adults with ASD, is broadly a psychoeducation and condition management program. It includes an array of strategies (i.e., managing and responding to criticism, breathing exercises, progressive muscle relaxation) designed to help individuals manage stress, improve social skills, and cope with everyday problems, as well as a psychoeducation component to help individuals with ASD learn about their condition. Like CET, EST is delivered over an 18-month period.

3.3.3 Stress Management Components of CET and EST

While not the primary focus of either treatment program, both CET and EST include the same stress and emotion management components in either a group (CET) or individual (EST) therapy context. These basic stress management components cover three key aspects of stress management: (1) early awareness of distress; (2) increased recognition of potentially distressing

situations; and (3) implementation of active and passive coping strategies. Participants are taught to recognize physical (e.g., indigestion, teeth grinding, feelings of pressure or pain in chest), behavioral (e.g., increased irritability, disrupted sleep patterns, quick mood changes), emotional (e.g., feeling out of control, consistent feelings of anger, emotional ups and downs), and cognitive (e.g., fuzzy or foggy thinking, rumination, trouble remembering things) signs or cues of distress. They are then taught to recognize situations that often contribute to the identified signs or cues of distress and to use basic social skills to avoid conflict, modify responsibilities, and be positive in these situations. Finally, they are taught both active (e.g., exercise, muscle relaxation, diaphragmatic breathing, prayer) and passive (e.g., avoiding stressful situations, watching TV, rest and relaxation) strategies to cope with distress.

3.4 MEASUREMENTS

This study utilized different independent and dependent variables for Aim #1 and Aim #2, and examined biological stress response and psychosocial stress separately for each analytic aim (see Table 1, below). For Aim #1, Analysis #1, the independent variable was group (ASD vs. control) and the dependent variable was biological stress response. For Aim #1, Analysis #2, the independent variable was group (ASD vs. control) and the dependent variable was psychosocial stress. For Aim #2, Analysis #1, the independent variable was biological stress response and the dependent variable was social functioning. For Aim #2, Analysis #2, the independent variable was psychosocial stress and the dependent variable was social functioning.

For the ASD cohort, novel measures included heart rate, systolic blood pressure, diastolic blood pressure, salivary cortisol, the Perceived Stress Scale (Cohen & Janicki-Deverts, 2012;

Cohen & Williamson, 1988), the Stress Survey Schedule (Groden et al., 2001), and the Wisconsin Activities of Daily Living Scale (Maenner et al., 2013; Smith et al., 2012). Measures obtained through the CET and EST trial included the Global Assessment Scale (Endicott, Spitzer, Fleiss, & Cohen, 1976), the Social Adjustment Scale II (Schooler, Weissman, & Hogarty, 1979), and the Social Responsiveness Scale (Constantino, 2002). These measures were obtained from data collected during the most recent study visit. For healthy volunteers, all measures were collected during a single study visit. Each of these key variables is described below and in Table 1.

Table 1. *Measures Associated with the Specific Aims of this Research*

Aim	Independent Variable	Dependent Variable
<u>Aim #1, Analysis #1:</u> Identify differences in biological stress response among treatment-exposed adults with ASD and healthy volunteers.	<u>Construct:</u> Study Group <u>Existing Measure(s):</u> ASD vs. Control Group <u>New Measures:</u> None	<u>Concept:</u> Biological Stress Response <u>Existing Measure(s):</u> None <u>New Measure(s):</u> Cortisol reactivity, heart rate reactivity, systolic blood pressure reactivity, diastolic blood pressure reactivity
<u>Aim #1, Analysis #2:</u> Identify differences in psychosocial stress among treatment-exposed adults with ASD and healthy volunteers.	<u>Construct:</u> Study Group <u>Existing Measure(s):</u> ASD vs. Control Group <u>New Measures:</u> None	<u>Concept:</u> Psychosocial stress <u>Existing Measure(s):</u> None <u>New Measure(s):</u> Perceived Stress Scale, Stress Survey Schedule
<u>Aim #2, Analysis #1:</u> Examine the relationship between biological stress response and social functioning in treatment-exposed adults with ASD.	<u>Construct:</u> Biological Stress Response <u>Existing Measure(s):</u> None <u>New Measure(s):</u> Cortisol reactivity, heart rate reactivity, systolic blood pressure reactivity, diastolic blood pressure reactivity	<u>Concept:</u> Social Functioning <u>Existing Measure(s):</u> Global Assessment of Functioning, Social Responsiveness Scale, Social Adjustment Scale II <u>New Measure(s):</u> Wisconsin Activities of Daily Living
<u>Aim #2, Analysis #1:</u> Examine the relationship between psychosocial stress and social functioning in treatment-exposed adults with ASD.	<u>Construct:</u> Psychosocial stress <u>Existing Measure(s):</u> None <u>New Measure(s):</u> Perceived Stress Scale, Stress Survey Schedule	<u>Concept:</u> Social Functioning <u>Existing Measure(s):</u> Global Assessment of Functioning, Social Responsiveness Scale, Social Adjustment Scale II <u>New Measure(s):</u> Wisconsin Activities of Daily Living

“Existing Measures” are measures that were collected during the course of the clinical trial of CET and EST; “New Measures” are measures that were collected specifically for the purpose of this research.

3.4.1 Stress

All measures of biological stress response and psychosocial stress were newly collected data for the purpose of this research. Biological stress response and psychosocial stress were analyzed separately for the purpose of this study.

Description of experimental context. Measures of biological stress response and psychosocial stress were collected before (salivary cortisol), during (heart rate, systolic blood pressure, and diastolic blood pressure), and after (salivary cortisol, stressful life events, perceived stress) the Social Stress Recall Task. The Social Stress Recall Task is a social stress challenge task that has elicited reliable and statistically significant changes in biological stress response in caregivers of family members with Alzheimer's disease (Williams et al., 2010), healthy adults experiencing psychosocial distress (Kirby, Williams, Hocking, Lane, & Williams, 2006), and adults who have experienced stress as a result of discrimination (Richman, Bennett, Pek, Siegler, & Williams, 2007), among others. The development of this task was based on research indicating that tasks which elicit a strong emotional reaction to a stressor using recall also elicit cardiovascular and neuroendocrine reactivity (Krantz & Manuck, 1984).

The Social Stress Recall Task consisted of three segments: (1) a 10-minute rest condition; (2) a stressor condition in which subjects were asked to speak for five minutes using a prompt of "describe the three most challenging aspects of your life on a day-to-day basis"; and (3) a 5-minute recovery condition. If, during the stressor condition, the participant was unable to recall items that were stressful, standardized probes were used to assist participants in recalling events. These included probes such as: "try to think of a situation that you experienced that was stressful for you"; "can you tell me more about how that experience made you feel?"; and "tell me about the physical sensations you were aware of when you were experiencing stress." Debriefing was

done after the Social Stress Recall Task in order to ensure that the participant had not experienced too much stress when recalling their daily challenges.

Cardiovascular reactivity. Heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured at one-minute intervals using a portable Critikon Vital Signs Monitor during the Social Stress Recall Task. Data produced during the Social Stress Recall Task (described in greater detail below) were 10 measures of SBP, DBP, and HR during the rest condition, five measures of SBP, DBP, and HR during the stressor condition, and five measures of SBP, DBP, and HR during the recovery condition. For the purpose of this research, the first five minutes of the rest condition was treated as a habituation condition where participants adjusted to the pressure of and repeated measures with the blood pressure cuff before the rest condition was assessed. Data collected during the five-minute recovery condition after the Social Stress Recall Task were not analyzed in this research because they represent recovery from, not reactivity to, the stressor (Kirby et al., 2006; Williams et al., 2010). Thus, analysis of cardiovascular reactivity in this research includes a total of 5 measures of SBP, DBP, and HR during the rest condition and 5 measures of SBP, DBP, and HR during the stressor condition. Individual linear growth coefficients were calculated for SBP, DBP, and HR using hierarchical linear modeling in order to assess for cardiovascular reactivity, which is further discussed below.

Cortisol reactivity. Salivary “free” cortisol has been shown to track closely with plasma levels in both ambulatory and laboratory challenge paradigms, and collection of cortisol levels through saliva samples has been shown to be superior to blood sampling in psychoneuroendocrine research settings (Kirschbaum & Hellhammer, 1994). For the purposes of this study, salivary cortisol was assayed using radioimmunoassay (RIA) techniques. Salivary cortisol samples were collected using commercially available Salivette tubes before the Social

Stress Recall Task and at the end of testing after participants filled out questionnaires. Participants were instructed to fully wet a cotton swab contained within the Salivette tube by chewing on the swab. The process of wetting a cotton swab takes approximately one minute. Requiring that participants did not eat, drink, or smoke 30 minutes prior to collection of the sample ensured the quality and potency of the sample. Salivettes containing saliva samples were stored in a -20°C freezer based on established guidelines (Robins, Fraley, & Krueger, 2009) until shipment to the assay laboratory (Dr. Clemens Kirschbaum's laboratory at the Technical University of Dresden, Dresden, Germany). Samples were sent via express mail in order to ensure that they were not defrosted for more than four days in order to prevent growth of mold, which may compromise the interpretation of the assay (Robins et al., 2009). Assays were centrifuged by the assay laboratory after defrosting and assayed in batches of 65, balanced for ASD versus healthy volunteer group in order to avoid introduction of error due to assay batch variation. Cortisol levels were measured in micrograms/deciliter ($\mu\text{g}/\text{dl}$). In order to determine cortisol reactivity, the difference between cortisol levels collected before the Social Stress Recall Task and at the end of testing was completed was calculated.

Stressful life events. The degree to which individuals perceive life events to be stressful was measured with the Stress Survey Schedule (SSS) for Persons with Autism and Other Developmental Disabilities (Grodén et al., 2001), an instrument developed for measuring stress in the lives of people with autism and other developmental disabilities. The SSS is a 48-item questionnaire, scored on a 5-point Likert scale where higher scores indicate more stressful life events such that 1=None to Mild, 2=Mild to Moderate, 3=Moderate, 4=Moderate to Severe, and 5=Severe. The SSS measures stress across eight dimensions: (1) anticipation/uncertainty; (2) changes and threats; (3) unpleasant events; (4) pleasant events; (5) sensory/personal contact; (6)

food related activity; (7) social/environmental interactions; and (8) ritual related stress. Questions include items such as: “having a change in environment from familiar to unfamiliar”; “having a change in schedule or plans”; “being unable to assert oneself with others”; and “someone else making mistakes.” Participants completed the SSS using pen and paper, and assistance was offered to participants who needed help reading and interpreting questions. For participants who could not read and respond to the questionnaire themselves, participants were provided with response options to the questions, and questions were verbally presented to the participant. The participant was able to then indicate their answer choice, and research staff recorded their answer. Administration of the SSS takes between 10 and 15 minutes. The SSS has been found to be ecologically valid and to track closely with the clinical presentation of response to specific stressors, indicating high construct validity (Baron, Groden, Groden, & Lipsitt, 2006). Cronbach’s alpha reliability ranges from .81 to .90, indicating high internal consistency (Groden et al., 2001).

Perceived stress. Perceived stress was measured with the Perceived Stress Scale (PSS) (Cohen & Janicki-Deverts, 2012; Cohen & Williamson, 1988) which consists of 10 items that are evaluated on a 5-point Likert scale where higher scores indicated greater perceived stress such that 0=Never, 1=Almost Never, 2=Sometimes, 3=Fairly Often, and 4=Very Often. The items on the PSS tap the degree to which individuals feel that events in their lives are stressful. Questions include items such as: “in the last month, how often have you been upset because of something that happened unexpectedly?”; “in the last month, how often have you felt confident about your ability to handle your personal problems?”; and “in the last month, how often have you felt that things were going your way?” Participants completed the PSS using pen and paper, and assistance was offered to participants who needed help reading and interpreting questions. For

participants who could not read and respond to the questionnaire themselves, participants were provided with response options to the questions, and questions were verbally presented to the participant. The participant was able to then indicate their answer choice, and research staff recorded their answer. Administration of the PSS takes less than five minutes. Comparisons of the 10-item version with the original 14-item version of the scale reveal that the shorter version is psychometrically superior. Cronbach's alpha reliability ranges from .78 to .91 in numerous national surveys (Cohen & Janicki-Deverts, 2012; Cohen & Williamson, 1988). Patterns of correlations with other psychological scales, health measures, and health habits provide strong evidence for its construct validity.

3.4.2 Social Functioning

This dissertation conceptualizes social functioning in a way that takes into account key domains of ASD symptomatology and performance in social situations. This conceptualization more specifically creates a composite measure of key aspects of social functioning – including global functioning, social impairment, social disability, and daily living skills – that have been hypothesized in recent research to be central to well-being and independent functioning in ASD (Plimley, 2007). This conceptualization takes into account key social skills (i.e., social impairment, social disability) and adaptive functioning (i.e., daily living skills, global functioning) that contribute to overall social functioning.

Global functioning. Global functioning was measured with the Global Assessment Scale (Endicott et al., 1976), a single rating scale with structured anchors used to evaluate overall functioning during the last week prior to evaluation. Scores range from 1, which represents poor global functioning, to 100, which represents excellent global functioning. Global functioning

here is defined in terms of overall functioning and psychiatric wellness. For instance, scores from 91 to 100 represent “superior functioning in a wide range of activities, life’s problems never seem to get out of hand, is sought out by others because of his or her positive qualities” while scores from 1 to 10 represent “persistent danger or severely hurting self or others...OR persistent inability to maintain minimal personal hygiene OR serious suicidal act with clear expectation of death.” Current GAS scores were determined by trained clinical raters at the end of a broader structured clinical interview. This measure was collected as part of the ongoing clinical trial of CET and EST.

Social impairment. Social impairment was assessed with the Social Responsiveness Scale (SRS; Constantino, 2002), a 65-item parent-report rating scale, designed specifically for individuals with ASD, that measures autism symptom severity and social impairment across the domains of social awareness, social information processing, capacity for reciprocal social responses, social anxiety/avoidance, and characteristic autistic preoccupations/traits. The score generated by the SRS serves as an index for social deficits, with higher scores indicating greater social impairment. Questions include items such as: “Is socially awkward, even when he/she is trying to be polite,” “Has trouble keeping up with the flow of normal conversation,” and “Has a sense of humor, understands jokes.” Each question is rated on a four-point Likert scale where 1=Not True, 2=Sometimes True, 3=Often True, and 4=Almost Always True. Parents fill out the SRS using pen and paper, and administration of the SRS takes between 15 and 20 minutes. The SRS has high test-retest reliability (.88) in clinical subjects with ASD (Constantino et al., 2003). Evidence also suggests strong correlations between the SRS and the ADI-R ($r = 0.52$ to $r = 0.79$) and low correlation between the SRS and IQ ($r = -0.16$ to $r = -0.04$), indicating high construct

validity as a measure of autistic social impairment that is independent of overall intelligence. This measure was collected as part of the ongoing clinical trial of CET and EST.

Social disability. Disability with regard to social adjustment was assessed using the Social Adjustment Scale-II (SAS-II; Schooler et al., 1979), a structured interview-based measure that assesses social disability, and relative level of social functioning, in the domains of work, household life, family life outside of the household, social leisure, and personal well-being. The SAS-II contains 45 items covering the aforementioned domains. Scores on individual items range from 0 to 4, with higher scores representing more social disability. Five global ratings are also provided in the domains of work, household life, family life outside of the household, social leisure, and general social adjustment, based on scores across the entire interview. Scores on global composites range from 0 to 6, with higher scores representing more social disability. The SAS-II takes about 20 minutes to complete. The SAS-II has high internal consistency ($\alpha = .92$ to $.99$) in psychiatric populations (Bellack, Morrison, Mueser, Wade, & Sayers, 1990; Davies, Bromet, Schulz, & Dunn, 1989; Glazer, Aaronson, Prusoff, & Williams, 1980; Schooler et al., 1979). This measure was collected as part of the ongoing clinical trial of CET and EST.

Daily living skills. Independence in activities of daily living were assessed with the Wisconsin Activities of Daily Living Scale (W-ADL; Maenner et al., 2013; Smith et al., 2012), a 17-item measure designed specifically for adults with developmental disabilities, including autism, which assesses daily living skills across the domains of personal care, housekeeping, and meal-related activities. Questions where individuals are asked to rate their level of independence include items such as: “Doing laundry, washing and drying,” “Mixing and cooking simple foods, fry eggs, make pancakes, heat food in microwave, etc.,” and “Doing errands, including shopping in stores.” Each item is rated on a three-point Likert scale, where 0=Does not do at all; 1=Does

with help, and 2=Independent or does on own. Higher total scores represent greater independence. Participants completed the W-ADL using pen and paper, and assistance was offered to participants who needed help reading and interpreting questions. For participants who could not read and respond to the questionnaire themselves, participants were provided with response options to the questions, and questions were verbally presented to the participant. The participant was able to then indicate their answer choice, and research staff recorded their answer. Administration of the W-ADL takes less than five minutes. Cronbach's alpha for total scores range from .90 to .94 across multiple measurement occasions, indicating high internal consistency (Maenner et al., 2013; Smith et al., 2012). This measure was newly collected data for the purpose of this research.

3.4.3 Creation of Composite Indices

This research conceptualized biological stress response, psychosocial stress, and social functioning as three constructs, and multivariate composite indices were created to represent these constructs in order to conserve power by avoiding excessive univariate inference testing. The creation of composite indices for biological stress response, psychosocial stress, and social functioning is described below. Internal consistency of composite indices (biological stress composite, psychosocial stress composite, social functioning composite) was verified in order to estimate the reliability of these measures, and is described in greater detail along with the preliminary analyses, below.

Biological stress response. Biological stress response was measured using a composite variable of cortisol reactivity and cardiovascular reactivity. Cortisol reactivity was measured as the difference between salivary cortisol level at the beginning of testing and before the Social

Stress Recall Task (pre-test cortisol) and salivary cortisol level at the end of testing (post-test cortisol). Cardiovascular reactivity was measured individually for SBP, DBP, and HR. In order to obtain change scores (reactivity) for SBP, DBP, and HR, individual linear growth coefficients were calculated for each variable from an unconditional linear growth model, $Y_{ti} = \pi_{0i} + \pi_{1i}a_{ti} + e_{ti}$, where π_{1i} represents the linear rate of increase in the cardiovascular reactivity (i.e., SBP reactivity, DBP reactivity, or HR reactivity) variable during the social stress task for person i . For the purpose of this research, time was coded from zero to nine, where each integer represents one minute. The rest condition was comprised of times 0, 1, 2, 3, and 4 while the stressor condition was comprised of times 5, 6, 7, 8, and 9. Linear growth coefficients were calculated for SBP, DBP, and HR for each participant based on these growth models. Linear growth coefficients were used rather than simple window averaging or subtraction within the rest or stressor condition in order to account for individual differences in change trajectories for SBP, DBP, and HR, a method that has become the new field standard for analysis of cardiovascular reactivity data (Llabre, Spitzer, Siegel, Saab, & Schneiderman, 2004). Individual growth scores on measures of SBP reactivity, DBP reactivity, HR reactivity, and cortisol reactivity were converted to a common metric (z-scale) and averaged together to create a composite index of biological stress response. Higher scores on the biological stress composite indicated greater biological stress response.

Psychosocial stress. Individual summed scores on measures of stressful life events (SSS) and perceived stress (PSS) were converted to a z-metric and averaged together to create a composite index of psychosocial stress. Higher scores on the psychosocial stress composite indicate greater psychosocial stress.

Social functioning. Individual summed scores on measures of global functioning (GAS), social impairment (SRS), social disability (SAS-II), and daily living skills (W-ADL) were converted to a common metric (z-scale) and averaged together to create a composite index of social functioning. Higher scores on the social functioning composite indicate better social functioning. As such, the SAS-II and the SRS were reverse coded before the social functioning composite was created.

3.5 STUDY PROCEDURE

Participants with and without an ASD diagnosis were recruited for this study. Potential participants with an ASD diagnosis were recruited from a clinical trial of CET and EST. These potential participants were approached by study staff from the CET and EST trial, both via recruitment letter and via discussions with study clinicians. Because these participants had already been screened for the clinical trial of CET and EST, screening procedures were unnecessary for participants with ASD.

Potential participants who would serve as healthy volunteers for this study were recruited via a database of participants who have already served as healthy volunteers for studies of CET and EST and participants who has served as healthy volunteers for previous ASD studies in the University of Pittsburgh Center for Excellence in Autism Research. Diagnostic interviews for healthy volunteers were carried out using the Structured Clinical Interview for DSM-IV (First et al., 2002) by research staff supervised by diagnosticians. This interview consisted of a series of questions designed to indicate if the participant was experiencing any mental health concerns. This interview took between 30 and 60 minutes. If, at the end of this interview, study staff

believed that there was a possibility that a potential participant qualified for a mental health diagnosis, the participant was referred for treatment to Western Psychiatric Institute and Clinic. In this study, no such referrals were made for any participants who served as healthy volunteers.

When participants arrived at the clinic for data collection, they were greeted and brought back to the testing room. Then, the study was discussed in detail, the consent form was reviewed, questions and concerns were discussed in detail, and informed consent was given. After the consent process, all participants provided a saliva sample. Then, for both adults with ASD and healthy volunteers, a blood pressure cuff was attached to the participant's arm, and the participant's blood pressure was then measured a total of 20 times for a total of 20 minutes (once per minute for 20 minutes), during which the Social Stress Recall Task was administered (described above). Next, all participants filled out a series of questionnaires, which were administered in a standardized order and are detailed in Table 2, below. Finally, participants supplied the second of the two saliva samples. At the end of the study visit, participants were debriefed about their experiences during the data collection, and any questions were discussed in detail. The clinic visit took between 45 minutes and 2.5 hours, and healthy volunteers generally completed the assessments more quickly than adults with ASD.

Table 2. *Order of Study Measures during Clinic Visit*

Measure	ASD	Healthy Volunteer
Pre-test saliva sample	1	1
Resting cardiovascular measures (10 measures of HR, SBP, and DBP)	2	2
Stressor cardiovascular measures (5 measures of HR, SBP, and DBP)	3	3
Recovery cardiovascular measures (5 measures of HR, SBP, and DBP)	4	4
Perceived Stress Scale	5	5
Stress Survey Schedule	6	6
Williams LifeSkills Questionnaire ^A	7	7
Interpersonal Support Evaluation List ^A	8	8
Wisconsin Activities of Daily Living	9	9
Service Use Survey ^A	10	10
Pittsburgh Sleep Quality Index ^A	11	11
Health Assessment Questionnaire ^A	12	12
World Health Quality of Life – BREF ^A	previous visit	13
Social Responsiveness Scale	previous visit	--
Social Adjustment Scale – II	previous visit	14
Brief Psychiatric Rating Scale	previous visit	15
Global Assessment Scale	previous visit	16
Post-test saliva sample	13	17

Note. All measures were collected during the clinic visit for this study unless otherwise noted (“previous visit”). If measures were not collected at the clinic visit for this study, they were collected during the most recent, previous study visit (for the clinical trial of EST and CET).

^AMeasure was collected but not used for the purpose of this research.

3.6 DATA ANALYSIS

The data analysis plan for this research tested the hypotheses and specific aims outlined in Chapter 2 to: (1) assess differences in biological stress response between individuals with ASD and healthy volunteers; (2) assess differences in psychosocial stress between individuals with ASD and healthy volunteers; (3) examine the relationship between biological stress response and social functioning in individuals with ASD; and (4) examine the relationship

between psychosocial stress and social functioning in individuals with ASD. This section provides a description of the statistical analyses used in order to address these aims, as well as a power analysis outlining the feasibility of this research with the available sample size. Results of these analyses are detailed in Chapter 4.

3.6.1 Sample Description

Descriptive statistics were reported for age, race, gender, intelligence quotient (IQ), as measured by the Wechsler Abbreviated Scale of Intelligence (Wechsler, 2008), employment, education, and independent living. For continuous variables (age and IQ), descriptive statistics including mean, standard deviation, and range were reported. For categorical variables (race, gender, employment, education, and independent living), frequency and percentage were reported. All demographic statistics were reported by study group (i.e., ASD and control group).

3.6.2 Preliminary Analyses

Prior to investigating the primary analytic aims of this research, preliminary analyses were conducted to verify internal consistency among study measures, check assumptions associated with the statistical tests linked to each study aim, inform the primary analyses about the potential effects of demographic heterogeneity, and ensure that the Social Stress Recall Task elicited statistically significant changes in biological stress response.

First, the internal consistency of individual measures (PSS, SSS, SAS-II, and W-ADL) and composite measures (biological stress composite, psychosocial stress composite, social functioning composite) were verified in order to estimate the reliability of these measures.

Cronbach's alpha (α) was used to measure internal consistency, with estimates of $\alpha \geq .80$ considered to be indicative of high internal consistency, $\alpha \geq .70$ considered to be indicative of adequate internal consistency, and $\alpha \geq .60$ considered to be indicative of minimally adequate internal consistency (Nunnally, 1978). A combined sample of adults with ASD and healthy volunteers was used to compute α for all Aim #1 variables, the stress measures (PSS, SSS, biological stress composite, psychosocial stress composite), while a sample of only adults with ASD was used to compute α for all social functioning measures (W-ADL, SAS-II, social functioning composite) used in Aim #2, given the exclusive focus of this aim on the participants with ASD.

Second, the distribution of continuous variables was examined in order to ensure that they met the assumptions of parametric testing. These analyses were conducted by calculating skewness statistics in order to assess skewed data distributions and visually inspecting histograms of data distributions in order to identify other non-normal (e.g., bimodal, uniform, exponential) distributions. Individual cases of outliers were identified if their score on a single measure was 2.0 times the interquartile range (the difference between scores of the 3rd and 1st quartiles) of the distribution of scores in the sample (Hoaglin, Iglewicz, & Tukey, 1986). Skewness statistics greater than 1.0 were considered to be indicative of moderately skewed distributions (Mardia, 1970) and were accordingly transformed in order to meet the assumptions of parametric testing. For the purpose of this research, winsorization procedures were used to transform outlier cases to within 2.0 times the interquartile range of the data distribution by setting the value of the outlier to the next closest value within 2.0 times the interquartile range (Dixon & Tukey, 1968).

Third, while it was expected that no systematic group differences in demographic variables exist between the ASD and healthy volunteer groups, the effects of study group (i.e., ASD or healthy volunteer) differences in demographics were examined. Salient demographic variables for which there were differences between the ASD and healthy volunteer groups were determined before conducting analyses and included as covariates. For Aim #1, group differences between the ASD and healthy volunteer groups were assessed using a t-test for age and IQ and a chi-square test for race and gender. Any demographic variables for which there were significant group differences were included as covariates.

Fourth, since biological stress response, psychosocial stress, or social functioning may be related to age, gender, race, IQ, or treatment exposure, the relationship between the aforementioned potential demographic or clinical confounders and the independent variables (biological stress response and psychosocial stress) and the dependent variable (social functioning) (Aim #2) were individually assessed using a zero-order correlation for age, IQ, and treatment exposure and a point bi-serial correlation for race and gender. These analyses helped to determine which potential demographic or clinical confounders are salient and thus needed to be included in analyses for Aim #2 and in order to account for shared variance between these variables and the main independent and dependent variables of this aim. If the correlation between a demographic or clinical confounder and an independent or dependent variable was significant at the trend level (i.e., $p < 0.10$), the variable was included in and controlled for in these analyses.

Finally, the effectiveness of the Social Stress Recall Task at eliciting cardiovascular reactivity to the stressor condition was assessed after the first four participants were tested, and the task was found to elicit a statistically significant change in mean SBP, $t = 6.171$, $p = 0.009$,

and mean DBP, $t = 7.834$, $p = 0.004$, and a trend towards a statistically significant change in mean HR, $t = 2.763$, $p = 0.069$, between the rest condition and stressor condition. Then, these effects were verified in the final sample in order to ensure that this task contributed to statistically significant changes in cardiovascular and cortisol reactivity measures over time using individual growth models to confirm statistically significant linear growth over time. In addition, a paired sample t-test was used to confirm differences between pre-test and post-test cortisol levels.

3.6.3 Analyses of Specific Aims and Hypotheses

The hypotheses associated with the specific aims of this project were tested using separate procedures. All analyses were conducted using R version 3.2.0 (R Core Team, 2015), with packages nlme (Pinheiro, Bates, DebRoy, Sarkar, & R Core Team, 2015), Amelia (Honaker, King, & Blackwell, 2011), Hmisc (Harrell Jr, 2008), psych (Revelle, 2014), car (Fox & Weisberg, 2011), MASS (Venables & Ripley, 2002), lsmeans (Lenth, 2013), multcomp (Hothorn, Bretz, & Westfall, 2008), and QuantPsyc (Fletcher, 2008). Analyses are described below.

Aim #1: Identify differences in stress among treatment-exposed adults with ASD (n=40) and healthy volunteers (n=25) by examining: (1) cortisol reactivity and cardiovascular reactivity during both a stressor and rest condition in a social stress challenge task; and (2) self-reported psychosocial stress.

Data collected from a single timepoint were used to assess differences between treatment-exposed adults with ASD and healthy volunteers measured in terms of biological stress response

and psychosocial stress. In addition, exploratory analyses examined group differences in resting SBP, DBP, HR, and cortisol levels.

Biological stress response. In order to assess group differences in biological stress response, cardiovascular reactivity and cortisol reactivity were assessed using analysis of variance procedures, adjusting for salient demographic factors. The main independent variable in the ANOVA model was study group (i.e., ASD or control). The main dependent variable was biological stress response composite score. Correction for multiple inference testing was not conducted due to the presence of only two study groups.

Psychosocial stress. In order to assess group differences in psychosocial stress, stressful life events and perceived stress were assessed using ANOVA procedures, adjusting for salient demographic factors. The main independent variable in the ANOVA model was study group (i.e., ASD or control). The main dependent variable was psychosocial stress composite score. Correction for multiple inference testing was not conducted due to the presence of only two study groups.

Exploratory analyses. An additional series of post-hoc exploratory analyses was conducted in order to test whether adults with ASD and healthy volunteers differed on resting (pre-stress condition) biological stress measures, adjusting for salient demographic factors. These exploratory analyses included a series of one-way ANOVA tests for resting SBP, resting DBP, resting HR, and resting cortisol. For cardiovascular measures, mean resting values were calculated as an average of the rest period for SBP, DBP, and HR.

Aim #2: Examine the relationship between stress and social functioning – including global functioning, social impairment, social disability, and daily living skills – in treatment-exposed adults with ASD (n=40) via the use of multivariate analysis to predict adult outcomes from stress.

Two separate models were created: one for biological stress response and one for psychosocial stress.

Biological stress response. First, the bivariate association between biological stress response and social functioning composite score was tested using a series of Pearson's correlation analyses. Then, for biological stress response variables for which there was a significant association at the bivariate level, the relationship between biological stress response and social functioning in treatment-exposed adults with ASD was examined using hierarchical linear regression predicting social functioning from biological stress response, after potential demographic confounders. The main independent variable was biological stress response. The main dependent variable was social functioning. Salient demographic variables were entered into the model in step one, and the biological stress response composite score was entered into the model in step two.

Psychosocial stress. First, the bivariate association between psychosocial stress composite score and social functioning composite score was tested using a series of Pearson's correlation analyses. Then, if a significant association existed between psychosocial stress and social functioning at the bivariate level, the relationship between psychosocial stress and social functioning in treatment-exposed adults with ASD was examined using hierarchical linear regression predicting social functioning from psychosocial stress. The main independent variable was psychosocial stress. The main dependent variable was social functioning. Salient

demographic variables were entered into the model in step one, and the psychosocial stress composite score was entered into the model in step two.

Exploratory analyses. An additional series of post-hoc exploratory analyses was conducted in order to test the associations between all stress variables and all social functioning variables. The main independent variables of these models were stress response measures. The main dependent variables of these models were social functioning measures. Stress response variables included SBP reactivity, DBP reactivity, HR reactivity, cortisol reactivity, PSS, and SSS. Social functioning variables included the SAS-II, GAS, and SRS. First, the bivariate association between stress and social functioning variables was tested using a series of Pearson's correlation analyses. Then, for variables for which there was a statistically significant association at the bivariate level, a series of hierarchical multiple regression analyses was run in order to test the association between these variables, predicting social functioning measures from stress response measures. Salient demographic variables were entered into the model in step one, and the stress measures were entered into the model in step two.

3.6.4 Approach to Missing Data

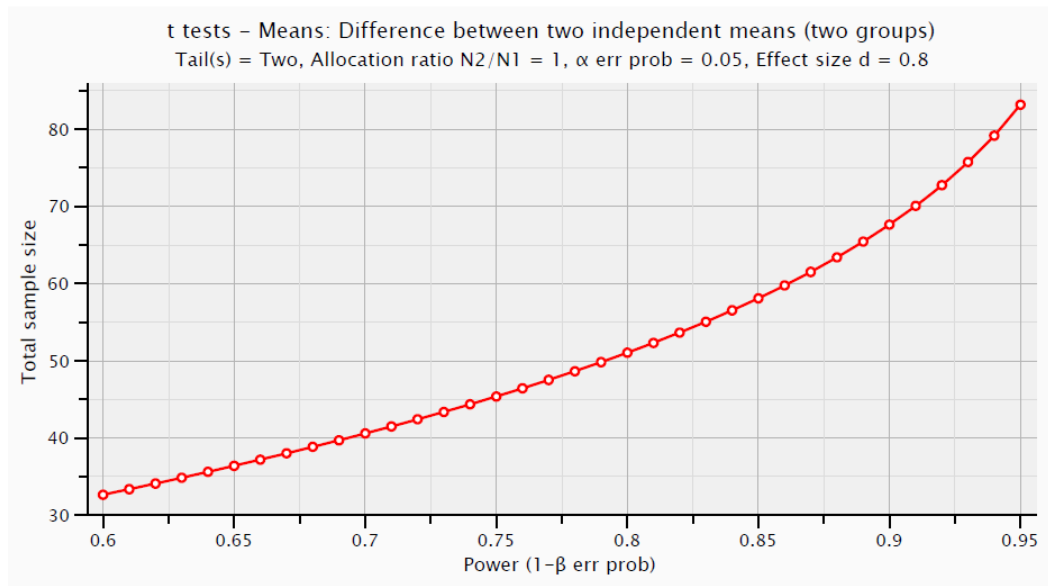
Because data in this research study were collected during a single study visit, it can be assumed that missing data are likely to be missing completely at random, not as a result of systematic differences in attrition. Of course, data may be missing because of lack of response. Therefore, patterns of nonresponse were assessed and the relative randomness of missing data were determined. Data may be missing at random (MAR), in which the distribution of missingness does not depend on the missing parts of data. Data may also be missing completely at random (MCAR), in which the distribution of missingness does not depend on either the

missing parts of the data or the observed parts of the data (Schafer & Graham, 2002). This was assessed using Little's MCAR test (Little, 1988). Recent research on missing data suggests that when data are MAR or MCAR, the best approach for handling missing data is to impute using the expectation-maximization algorithm, which results in less biased parameter estimates than mean or regression imputation (Dempster, Laird, & Rubin, 1977; Honaker et al., 2011; Schafer & Graham, 2002; Schlomer, Bauman, & Card, 2010).

3.6.5 Power and Sample Size

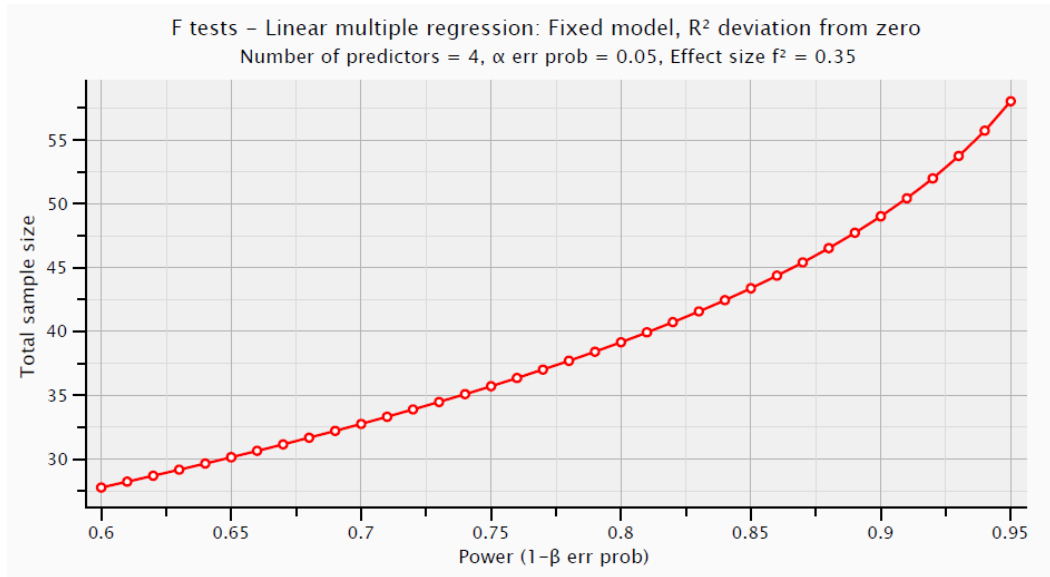
Estimates of the sample size requirements for the proposed study were calculated using standard procedures (Cohen, 1988), assuming that the criterion for statistical significance is set at $\alpha = .05$ and for statistical power $(1-\beta) = .80$ or more. All power analyses were conducted *a priori* using with G*Power 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007). Based on these criterion, approximately 26 participants would be needed per group in order to detect a large effect size for the difference in perceived stress and stress reactivity between patients with ASD and healthy volunteers (Aim #1, Figure 1).

Figure 1. *Power Analysis for Aim #1*



Based on a four predictor model using linear multiple regression and set at the aforementioned criteria, 40 participants would be required to detect a large effect size for the relationship between stress and adult outcomes ($f^2 = .35$; Aim #2, Figure 2).

Figure 2. Power Analysis for Aim #2



4.0 RESULTS

This chapter presents a series of statistical analyses designed to address the primary questions of this research. These questions focus on: (1) identifying differences in stress among treatment-exposed adults with ASD and healthy volunteers; and (2) examining the relationship between stress and social outcomes in treatment-exposed adults with ASD. This chapter begins with a presentation of the demographic characteristics of the adults with ASD and healthy volunteers who participated in this research. Then, it proceeds with a series of preliminary analyses designed to check the internal consistency of study measures and composite variables, verify that data met criteria for parametric testing, investigate potential demographic and clinical confounds with primary independent and dependent variables, and confirm that the Social Stress Recall Task elicited statistically significant changes in biological stress response. This chapter concludes with a presentation of results from the analyses associated with the primary study aims and hypotheses.

4.1 SAMPLE CHARACTERISTICS

A total of 40 adults with ASD and 25 healthy volunteers participated in this research. Demographic characteristics of participants with ASD and healthy volunteers are presented in Table 3. Most participants were male, of European American descent, and in their mid-twenties.

Of the participants with ASD, few had completed college or were employed, although they were, on average, of normal intelligence. Adults with ASD and healthy volunteers did not differ significantly with regard to biological sex, race, age, or IQ, suggesting that group matching was successful. As expected, adults with ASD and healthy volunteers did differ significantly in terms of employment, education, and independent living.

Table 3. *Participant Demographics*

Variable	M (SD) / % (N)			<i>p</i> ^a
	ASD (<i>N</i> = 40)	Control (<i>N</i> = 25)	Combined (<i>N</i> = 65)	
Age	24.20 (6.95)	24.84 (3.69)	24.45 (5.89)	.673
IQ ^b	106.53 (15.33)	110.60 (14.67)	108.09 (15.10)	.293
Male	90.00 (36)	84.00 (21)	87.69 (57)	.743
European American	82.50 (33)	68.00 (17)	76.92 (50)	.295
Employed ^c	47.50 (19)	84.00 (21)	61.54 (40)	.007**
College Graduate	22.50 (9)	60.00 (15)	36.92 (24)	<.001***
Lives Independently ^d	17.5 (7)	88.00 (22)	44.62 (29)	.005**

Note. ASD = autism spectrum disorder, M = mean, N = number

^a Fisher's exact test or independent *t*-test, two-tailed, for significant differences between adults with ASD or healthy volunteers.

^b Based on the full Wechsler Adult Intelligence Scale-Revised

^c Based on any paid employment

^d Lives either alone or with non-relatives

* *p* < .05, ** *p* < .01, ****p* < .001

4.2 PRELIMINARY ANALYSES

4.2.1 Internal Consistency of Study Measures and Composite Variables

Preliminary analyses began by first performing a series of tests to check the internal consistency of the primary study measures and the composite variables created from them. These

analyses were conducted in order to estimate the reliability of study measures. Cronbach's alpha (α) was used to measure internal consistency, with estimates $\alpha \geq .60$ considered to be indicative of minimally adequate internal consistency for the purpose of this study (Nunnally, 1978). A combined sample of adults with ASD and healthy volunteers was used to compute α for all Aim #1 variables, the stress measures (PSS, SSS, biological stress composite, psychosocial stress composite), while a sample of only adults with ASD was used to compute α for all social functioning measures (W-ADL, SAS-II, social functioning composite) used in Aim #2, given the exclusive focus of this aim on the participants with ASD.

Perceived Stress Scale. Table 4 presents internal consistency estimates for the PSS using the combined sample of adults with ASD and healthy volunteers. As noted in Table 4, the PSS exhibited high internal consistency ($\alpha = .91$), with all items displaying item-total correlations above .15.

Table 4. *Perceived Stress Scale Internal Consistency*

Item	α	Item Total	α Without
Total	.91		
1. In the last month, how often have you been upset because of something that happened unexpectedly?		.65	.90
2. In the last month, how often have you felt that you were unable to control the important things in your life?		.77	.89
3. In the last month, how often have you felt nervous and "stressed"?		.66	.90
4. In the last month, how often have you felt confident about your ability to handle your personal problems?		.63	.90
5. In the last month, how often have you felt that things were going your way?		.39	.91
6. In the last month, how often have you found that you could not cope with all the things that you had to do?		.79	.89
7. In the last month, how often have you been able to control irritations in your life?		.64	.90
8. In the last month, how often have you felt that you were on top of things?		.60	.90
9. In the last month, how often have you been angered because of things that were outside of your control?		.76	.89
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?		.78	.89

Note. Analyses were conducted on the combined sample of adults with ASD (N = 40) and healthy volunteers (N = 25).

Stress Survey Schedule. Table 5 presents internal consistency estimates for the SSS using the combined sample of adults with ASD and healthy volunteers. As noted in Table 5, the SSS exhibited high internal consistency ($\alpha = .97$), with all items displaying item-total correlations above .15.

Table 5. *Stress Survey Schedule Internal Consistency*

	α	Item Total	α Without
Total	.97		
1. Receiving a present		.43	.97
2. Having personal objects out of order		.61	.97
3. Waiting to talk about desired topic		.74	.97
4. Having a change in schedule or plans		.67	.97
5. Being in the vicinity of noise or disruption by others		.72	.97
6. Waiting for preferred events		.74	.97
7. Having a cold		.57	.97
8. Being touched		.41	.97
9. Having personal objects or materials missing		.46	.97
10. Having a change in task to a new task with new directions		.71	.97
11. Going to a store		.54	.97
12. Being prevented from completing a ritual		.77	.97
13. Having a change in environment from comfortable to uncomfortable		.72	.97
14. Being prevented from carrying out a ritual		.77	.97
15. Moving from one location to the next		.67	.97
16. Playing with others		.64	.97
17. Having a change in environment from familiar to unfamiliar		.67	.97
18. Receiving activity reinforcement		.62	.97
19. Having something marked as correct		.44	.97
20. Being in the vicinity of bright lights		.65	.97
21. Following a diet		.52	.97
22. Having unstructured time		.70	.97
23. Being allowed to attend a party or favored event		.50	.97
24. Receiving a reprimand		.49	.97
25. Transitioning from preferred to non-preferred activity		.74	.97
26. Being told "no"		.67	.97
27. Receiving criticism		.66	.97
28. Having something marked incorrect		.82	.97
29. Being interrupted while engaging in a ritual		.82	.97
30. Receiving hugs and affection		.37	.97
31. Having to engage in not-liked activity		.74	.97
32. Waiting in line		.69	.97
33. Being unable to communicate needs		.65	.97
34. Waiting at a restaurant		.51	.97
35. Going home (from school, to visit parents)		.51	.97
36. Waiting for transportation		.62	.97
37. Being unable to assert oneself with others		.51	.97
38. Needing to ask for help		.63	.97
39. Participating in group activity		.64	.97
40. Having a change in staff, teacher, or supervisor		.69	.97

	α	Item Total	α Without
41. Losing a game		.60	.97
42. Waiting for reinforcement		.70	.97
43. Feeling crowded		.67	.97
44. Someone else making a mistake		.61	.97
45. Receiving tangible reinforcement		.60	.97
46. Waiting for food		.69	.97
47. Waiting for routine to begin		.63	.97
48. Having a conversation		.70	.97
49. Receiving verbal reinforcement		.67	.97

Note. Analyses were conducted on the combined sample of adults with ASD (N = 40) and healthy volunteers (N = 25).

Waisman Activities of Daily Living. Table 6 presents internal consistency estimates for the W-ADL in adults with ASD. Because the W-ADL was designed to assess daily living skills in individuals with developmental disabilities who function along a broad continuum of ability, some items exhibited no variance (i.e., all participants rated 2 – “Independent or does on own”) in higher-functioning individuals with ASD who participated in this research because they were designed for lower-functioning individuals. These items included: “Washing/bathing”; “Grooming, brushing teeth, combing and/or brushing hair”; “Dressing and undressing”; “Toileting”; “Drinking from a cup”; and “Eating from a plate.” Because items with no variance cannot be included in calculations of Cronbach’s α (Nunnally, 1978), they were excluded from analysis. As noted in Table 6, the W-ADL exhibited high internal consistency ($\alpha = .81$), with all items displaying item-total correlations above .15.

Table 6. *Waisman Activities of Daily Living Internal Consistency*

Item	α	Item Total	α Without
Total	.81		
1. Making your own bed		.51	.80
2. Doing household tasks, including picking up around the house, putting things away, light housecleaning, etc.		.40	.81
3. Doing errands, including shopping in stores		.53	.79
4. Doing home repairs, including simple repairs around the house, non-technical in nature; for example, changing light bulbs or repairing a loose screw		.54	.79
5. Doing laundry, washing and drying		.55	.79
10. Preparing simple foods requiring no mixing or cooking, including sandwiches, cold cereal, etc.		.49	.81
11. Mixing and cooking simple foods, fry eggs, make pancakes, heat food in microwave, etc.		.58	.79
12. Preparing complete meal		.63	.78
13. Setting and clearing table		.33	.81
16. Washing dishes		.55	.79
17. Banking and managing daily finances, including keeping track of cash, checking account, paying bills, etc.		.26	.82

Note. Analyses were conducted on the sample of adults with ASD (N = 40).

Social Adjustment Scale-II. Table 7 presents internal consistency estimates of the total scale and seven subscales of the SAS-II in adults with ASD. Subscale α scores ranged from .33 to .80, and item-total correlations within subscales ranged from -.13 to .77. The overall α for the SAS-II indicates strong reliability, although the α scores for the interpersonal anguish, work affect, major roles, and self care subscales were low. Because a number of α scores for SAS-II subscales were not within the acceptable range, only the SAS-II total score was used in subsequent analyses. It is recognized that some item-total correlations were low and could be eliminated to improve the internal consistency of the total score. Such items were retained in order to maintain the original structure of the scale for comparability within the literature, and because the internal consistency of the SAS-II total score was adequate without their exclusion.

Table 7. *Social Adjustment Scale-II Internal Consistency*

	α	Item Total	α Without
Total	.81		
Interpersonal Anguish	.38		
Friction – Work (23)		.27	.30
Distress – Work (24)		-.02	.41
Worry – Household (41)		.32	.29
Guilt – Household (42)		.36	.32
Wronged – Household (43)		.33	.27
Friction – External (44)		-.13	.46
Worry – External (46)		.08	.39
Guilt – External (47)		.04	.39
Wronged – External (48)		-.11	.41
Sensitivity (57)		.21	.33
Loneliness (63)		.10	.37
Social Self-Appraisal (64)		.15	.36
Sexual Relations	.80		
Sexual Frequency (58)		.72	.69
Sexual Interest (59)		.51	.86
Sexual Problems (60)		.77	.59
Household/Family Relations	.75		
Friction (29)		.65	.62
Adaptability (30)		.53	.69
Communication (31)		.60	.65
Expressed Feelings (33)		.45	.74
Social Leisure	.80		
Leisure Activities (49)		.30	.81
Social Contacts – Frequency (50)		.68	.75
Social Contacts – Degree of Activity (51)		.59	.76
Social Comfort (53)		.59	.77
Interpersonal Contacts (54)		.56	.77
Communication (55)		.57	.77
Friction (56)		.53	.78
Work Affect/Vocational Functioning	.50		
Likes (25)		.35	.35
Interest (26)		.35	.35
Major Roles	.60		
Feelings of Adequacy (22)		.36	.56
Economic Adequacy (27)		-.01	.68
Household – Independence (32)		.14	.63
Work – Time Lost (20)		.61	.37
Work – Performance Adequacy (21)		.77	.24
Self Care	.33		
External Family - Independence (45)		.27	.04

	α	Item Total	α Without
Physical Health and Care (61)		.22	.18
Personal Appearance and Grooming (62)		.08	.43

Note. Analyses were conducted on the sample of adults with ASD (N = 40).

Biological stress response composite. Table 8 presents internal consistency estimates for the biological stress response composite, consisting of SBP reactivity, DBP reactivity, HR reactivity, and cortisol reactivity, in the combined ASD and healthy volunteer sample. Internal consistency estimates for the biological stress response composite were poor ($\alpha = .23$). While this research had anticipated creating a biological stress response composite, results of reliability testing indicate that the use of a biological stress response composite for this research is not warranted. These results may be explained by non-significant correlations between measures of biological stress response, with the exception of a significant correlation between HR and SBP (Table 9).

Table 8. *Biological Stress Response Composite Internal Consistency*

Item	α	Item Total	α Without
Total	.23		
Systolic blood pressure reactivity		.20	.06
Diastolic blood pressure reactivity		.10	.20
Heart rate reactivity		.18	.09
Cortisol reactivity		-.02	.35

Note. Analyses were conducted on the combined sample of adults with ASD (N = 40) and healthy volunteers (N = 25).

Table 9. *Correlations among Biological Stress Response Measures*

Variable	1	2	3	4
1. Systolic blood pressure reactivity	-			
2. Diastolic blood pressure reactivity	.13	-		
3. Heart rate reactivity	.25*	.07	-	
4. Cortisol reactivity	-.03	-.01	.01	-

Note. Analyses were conducted on the combined sample of adults with ASD (N = 40) and healthy volunteers (N = 25).

* $p < .05$

Psychosocial stress composite. Table 10 presents internal consistency estimates for the psychosocial stress composite in the combined ASD and healthy volunteer sample. Both the overall α and the item-total correlations for this composite were within the acceptable range, particularly considering that only two measures were used to compute this composite.

Table 10. *Psychosocial Stress Composite Internal Consistency*

Item	α	Item Total	α Without
Total	.73		
Perceived Stress Scale		.58	.58
Stress Survey Schedule		.58	.58

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40) and healthy volunteers (N = 25).

Social functioning composite. Table 11 presents internal consistency estimates for the social functioning composite in adults with ASD. For this composite measure, the overall α was not within the acceptable range ($\alpha = .54$). The W-ADL displayed a relatively low item-total correlation of .15. In order to improve the reliability of the social functioning composite, the W-ADL was dropped. This increased the reliability of the social functioning composite to $\alpha = .61$, which was deemed minimally acceptable for proceeding with primary analyses.

Table 11. *Social Functioning Composite Internal Consistency*

Item	α^a	Item Total ^a	α Without ^a	α^b	Item Total ^b	α Without ^b
Total	.54			.61		
Social Adjustment Scale-II		.44	.37		.52	.35
Wisconsin Activities of Daily Living		.15	.61		-	-
Global Assessment Scale		.35	.44		.40	.53
Social Responsiveness Scale		.38	.42		.34	.62

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40).

^a Values with W-ADL

^b Values without W-ADL

4.2.2 Verifying Assumptions of Parametric Testing

After the internal consistency of the primary study measures was examined, a series of analyses was conducted to examine the distribution of these measures and ensure that they met the assumptions of parametric testing. These analyses were conducted by calculating skewness statistics in order to assess skewed data distributions and visually inspecting histograms of data distributions in order to identify other non-normal (e.g., bimodal, uniform, exponential) distributions. Individual cases of outliers were identified if their score on a single measure was 2.0 times the interquartile range (the difference between scores of the 3rd and 1st quartiles) of the distribution of scores in the sample (Hoaglin et al., 1986). Skewness statistics greater than 1.0 were considered to be indicative of moderately skewed distributions (Mardia, 1970) and were accordingly transformed in order to meet the assumptions of parametric testing. For the purpose of this research, winsorization procedures were used to transform outlier cases to within 2.0 times the interquartile range of the data distribution by setting the value of the outlier to the next closest value within 2.0 times the interquartile range (Dixon & Tukey, 1968).

Table 12 presents descriptive statistics of primary study and demographic variables. Age was transformed using winsorization procedures for two data points at the top of the distribution.

Once transformed, this variable demonstrated a skewness statistic within the acceptable range. Thus, subsequent analyses make use of this winsorized variable. All other variables had distributional parameters suitable for parametric testing and required no transformation.

Table 12. *Descriptive and Skewness Statistics of Primary Study and Demographic Variables*

Variable	N	N _{miss}	M	SD	Min	Max	Skew (pre) ^d	Trans ^e	Skew (post) ^c
Age	65	0	24.45	5.89	18.00	44.00	1.31	win(2)	0.41
Full-Scale IQ ^a	65	0	108.09	15.10	80.00	138.00	0.06		
SBP reactivity ^b	65	0	0.00	1.00	-3.86	1.89	-0.91		
DBP reactivity ^b	65	0	0.00	1.00	-1.86	2.55	0.23		
HR reactivity ^b	65	0	0.00	1.00	-3.26	2.38	-0.03		
Cortisol reactivity ^{b,c}	64	1	0.00	1.00	-2.66	2.03	-0.44		
PSS	65	0	16.35	7.62	3.00	35.00	0.44		
SSS	65	0	103.88	33.35	52.00	195.00	0.51		
SAS-II ^c	35	5	1.28	0.40	0.36	2.06	-0.05		
GAS	40	0	53.46	8.25	32.00	80.00	0.41		
SRS	40	0	75.94	15.79	37.82	110.02	-0.26		

Note. Analyses conducted on the combined sample of treatment-exposed adults with ASD (N = 40) and healthy volunteers (N = 25). IQ = intelligence quotient. SBP = systolic blood pressure. DBP = diastolic blood pressure. HR = heart rate. PSS = Perceived Stress Scale. SSS = Stress Survey Schedule. SAS-II = Social Adjustment Scale-II. GAS = Global Assessment Scale. SRS = Social Responsiveness Scale.

^a Based on the full Wechsler Adult Intelligence Scale-Revised

^b z-metric

^c Missing data were imputed using expectation maximization

^d Skew (pre) refers to skewness before non-linear transformations. Skew (post) refers to skewness after non-linear transformation.

^e win(x) = winsorization procedure performed on x number of outliers

4.2.3 Identifying Potential Clinical and Demographic Confounds with Study Variables

After checking the internal consistency of key study and composite variables and ensuring that data met assumptions of parametric testing, a series of analyses were conducted in

order to identify potential clinical and demographic confounds with key study variables. These analyses are detailed separately for Aim #1 and Aim #2, below.

Aim #1. A series of analyses was conducted in order to ensure that groups did not differ significantly on potential demographic confounds. A two-sample t-test was used to test group differences on continuous potential demographic confounds (i.e., age, IQ). Chi-square procedures were used to test group differences on categorical potential demographic confounds (i.e., sex, race). As noted in Table 3, above, adults with ASD and healthy volunteers did not differ significantly in terms of age, IQ, biological sex, or race. Because of these findings, no confounding covariates were included in Aim #1 analyses.

Aim #2. A series of correlation analyses was conducted to examine the associations between primary study variables (i.e., SBP reactivity, DBP reactivity, HR reactivity, cortisol reactivity, psychosocial stress composite, social functioning composite) and potential clinical (i.e., treatment exposure) and demographic (i.e., age, sex, IQ, race) confounds in adults with ASD. As noted in the correlation matrix in Table 13, there was a trend-level relationship between cortisol reactivity and treatment exposure, indicating that cortisol reactivity decreased with treatment, as well as between psychosocial stress and treatment exposure, indicating that psychosocial stress increased with treatment. Because of this relationship and because exposure to either CET or EST may normalize stress response in a non-trivial way, treatment exposure was included as a covariate in all Aim #2 analyses. No other potential confounders of the relationship between stress and social functioning measures were observed.

Table 13. *Correlations between Primary Study Variables and Potential Demographic Confounds*

Variable	Age	IQ	Sex ^a	Race ^b	Treatment Exposure
SBP reactivity	-0.09	-0.07	0.07	-0.06	-0.06
DBP reactivity	-0.26	0.04	0.17	-0.02	0.03
HR reactivity	0.10	0.08	0.06	0.18	-0.03
Cortisol reactivity	0.25	0.18	-0.17	-0.04	-0.28 [†]
Psychosocial Stress	0.13	0.14	0.14	0.23	0.28 [†]
Social Functioning	-0.09	0.21	0.05	-0.10	-0.01

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40) and healthy volunteers (N = 25). IQ = intelligence quotient. SBP = systolic blood pressure. DBP = diastolic blood pressure. HR = heart rate.

^a Male = 0, Female = 1

^b European American = 0, Non-European American = 1

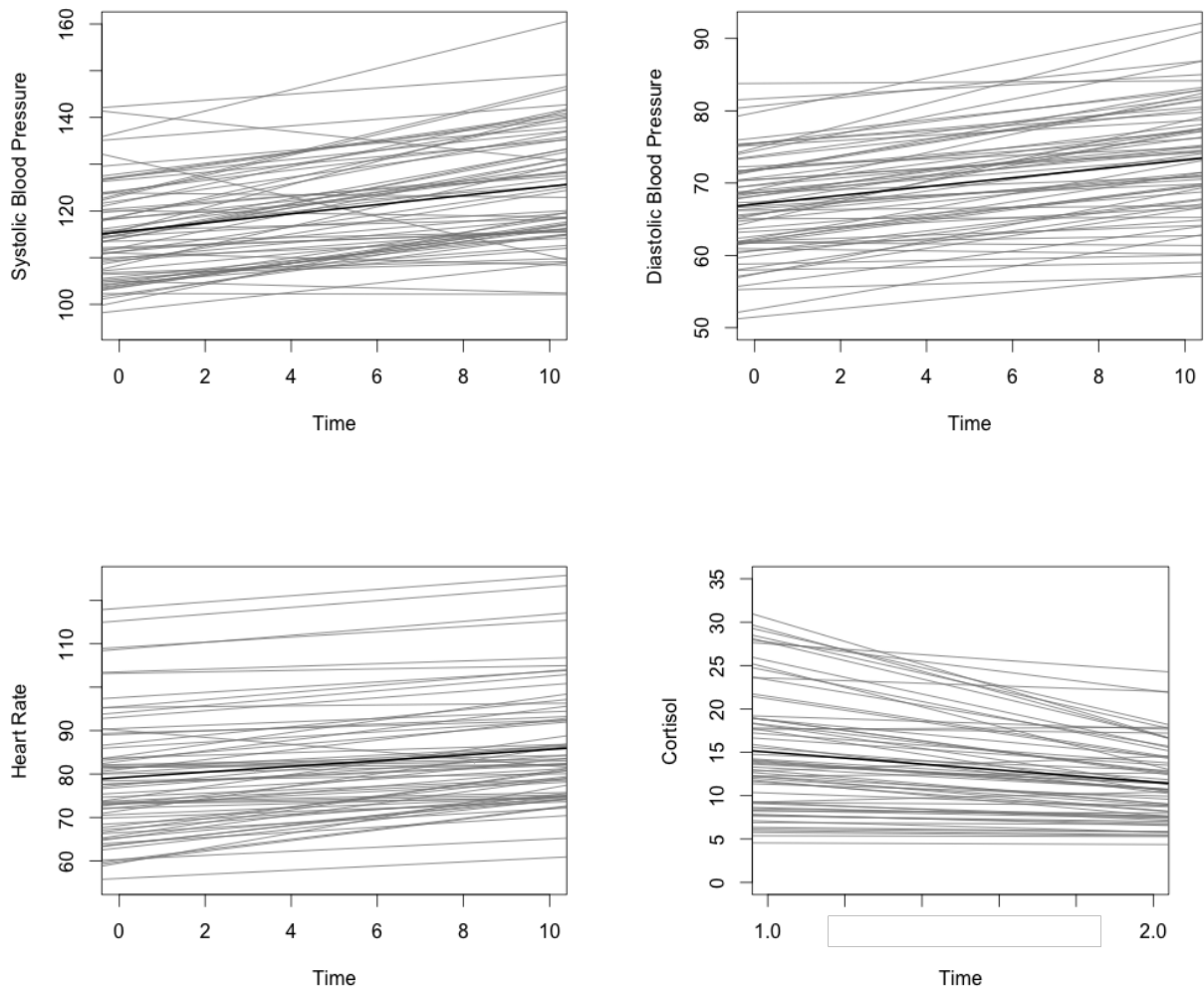
[†] $p < .10$, two-tailed

4.2.4 Social Stress Recall Task Effects

Before examining the hypotheses associated with the primary aims of this research, the effects of the social stress challenge task were examined in order to ensure that this task contributed to statistically significant changes in cardiovascular and cortisol reactivity measures over time. Results of individual growth curve models revealed statistically significant, positive linear growth over time for SBP ($\beta_{10} = .982, t = 6.76, p < .001$), DBP ($\beta_{10} = .612, t = 4.76, p < .001$), and HR ($\beta_{10} = .654, t = 6.86, p < .001$), confirming that this stress task produced increased cardiovascular response over time. A paired sample t-test was used to confirm differences between pre-test and post-test cortisol levels. This analysis revealed a statistically significant decrease, $t(64) = 3.296, p < .001$, in cortisol levels over time, indicating that the stress task produced decreased cortisol over time, a finding that was unexpected but that may be attributable to typical patterns of diurnal rhythm, or the daily pattern of change in cortisol levels, which indicate a generalized trajectory of increase in cortisol throughout the day (Smyth et al.,

1997; Stone et al., 2001). Linear growth trajectories for SBP, DBP, and HR, and cortisol reactivity in the combined sample of adults with ASD and healthy controls are displayed graphically in Figure 3. These trajectories based on individual linear growth coefficients and cortisol reactivity scores were then used in subsequent analyses to represent SBP reactivity, DBP reactivity, HR reactivity, and cortisol reactivity.

Figure 3. *Linear Growth Trajectories of Systolic Blood Pressure, Diastolic Blood Pressure, and Heart Rate and Cortisol reactivity over Time in the Combined Sample of Adults with ASD and Healthy Volunteers*



4.3 AIM #1: IDENTIFY DIFFERENCES IN STRESS RESPONSE AMONG TREATMENT-EXPOSED ADULTS WITH ASD HEALTHY VOLUNTEERS

4.3.1 Group Differences on Biological Stress Measures

Using ANOVA procedures, data were queried to determine if adults with ASD and healthy volunteers differed significantly in terms of SBP reactivity, DBP reactivity, HR reactivity, and cortisol reactivity. As noted in Table 14, adults with ASD had significantly greater SBP reactivity scores than healthy volunteers, $F(1, 63) = 4.95, p = .030$, but did not differ on DBP reactivity, $F(1, 63) = 1.46, p = .232$, HR reactivity, $F(1, 63) = 1.72, p = .194$, or cortisol reactivity, $F(1, 63) = .34, p = .564$ scores from healthy volunteers. Mean change scores, and their corresponding standard deviations, are presented in Figure 4. Additionally, in order to ensure that groups did not differ in their distribution of SBP reactivity, DBP reactivity, HR reactivity, and cortisol reactivity scores, scatter clouds of groups were visually examined (Figure 5). Based on these results, the hypothesis that there are significant differences between adults with ASD and healthy volunteers in terms of cardiovascular reactivity (Hypothesis 1a) is only partially supported as adults with ASD experienced significantly greater SBP reactivity than healthy volunteers, but no group differences in DBP reactivity or HR reactivity were present. The hypothesis that there are significant group differences between adults with ASD and healthy volunteers in terms of cortisol reactivity (Hypothesis 1b) is not supported.

Table 14. *One-Way Analysis of Variance for Biological Stress Variables by Group*

Source	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>p</i>	Cohen's <i>d</i> ^a
<i>Variable: SBP reactivity; ASD: M = 0.21, S.D. = 0.84; Control: M = -0.34, S.D. = 1.16</i>						
Between Groups	1	2.96	2.96	4.95	0.030*	0.54
Total	63	37.65	0.60			
<i>Variable: DBP reactivity; ASD: M = -0.12, S.D. = 1.01; Control: M = 0.19, S.D. = 0.97</i>						
Between Groups	1	0.20	0.20	1.46	0.232	0.31
Total	63	8.49	0.13			
<i>Variable: HR reactivity; ASD: M = 0.13, S.D. = 0.88; Control: M = -0.20, S.D. = 1.16</i>						
Between Groups	1	0.35	0.35	1.72	0.194	0.32
Total	63	12.70	0.20			
<i>Variable: Cortisol reactivity; ASD: M = 0.07, S.D. = 0.96; Control: M = -0.12, S.D. = 1.07</i>						
Between Groups	1	24.00	23.53	0.34	0.564	0.19
Total	63	4414	70.07			

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40) and healthy volunteers (N = 25). *df* = degrees of freedom. *SS* = sum of squares. *MS* = mean square. *SBP* = systolic blood pressure. *DBP* = diastolic blood pressure. *HR* = heart rate.

**p* < .05

^a Cohen's *d* is presented here for all biological stress response variables but should only be interpreted for *SBP* reactivity.

Figure 4. *Group Differences on Biological Stress Measures*

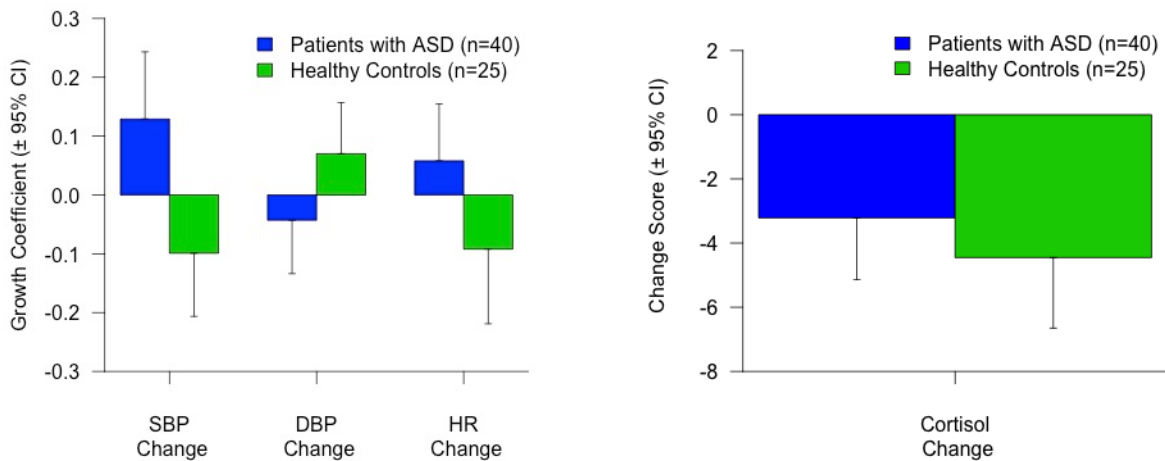
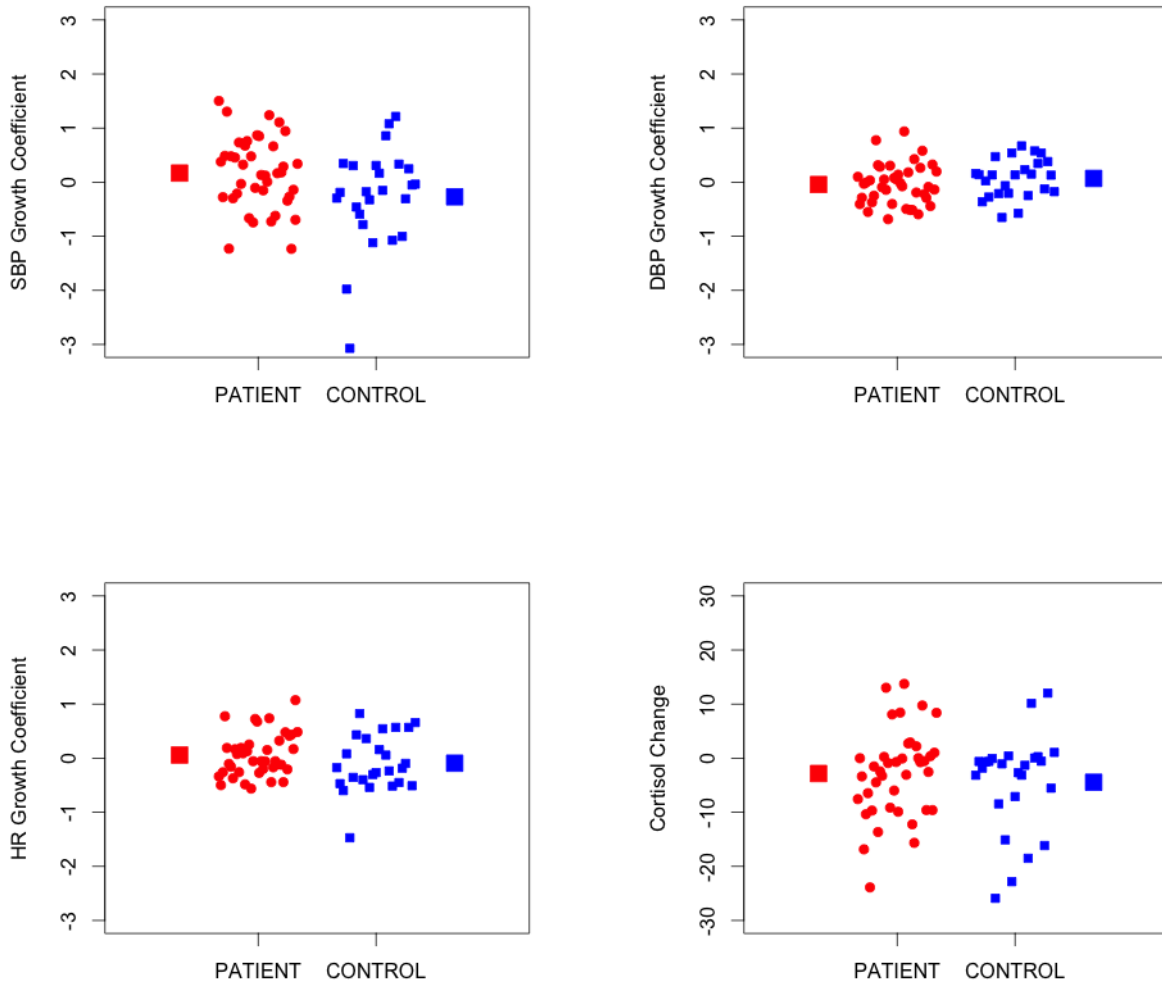


Figure 5. Group Scatter Clouds for Biological Stress Response Variables



4.3.2 Group Differences on Psychosocial Stress Composite

Data were queried using ANOVA procedures to determine if adults with ASD and healthy volunteers differed significantly in terms of psychosocial stress. As noted in Table 15, adults with ASD reported significantly greater psychosocial stress than healthy volunteers, $F(1,$

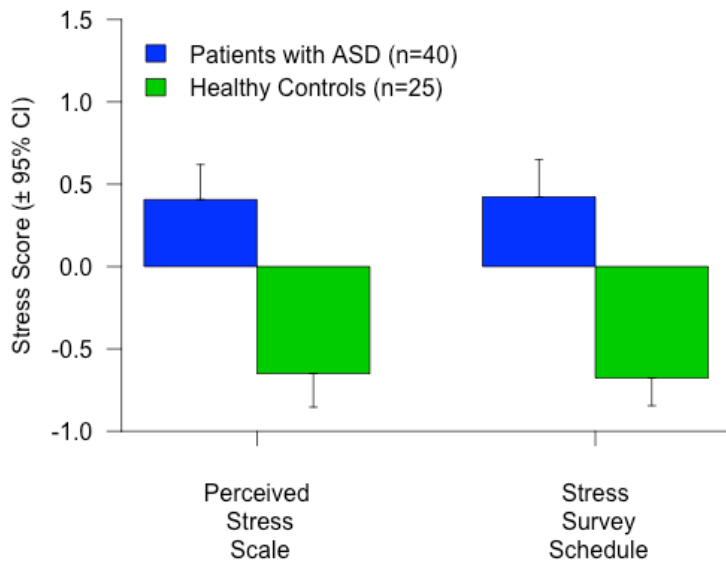
63) = 34.53, $p < .001$. Mean scores (z-metric), and their corresponding standard deviations, are presented in Figure 6. Based on these findings, the hypothesis that there are significant differences between adults with ASD and healthy volunteers in terms of psychosocial stress (Hypothesis 1c) is supported.

Table 15. *One-Way Analysis of Variance for Psychosocial Stress Composite by Group*

Source	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>p</i>	<i>Cohen's d</i>
<i>Variable: Psychosocial Stress; ASD: M = 0.41, S.D. = 0.75; Control: M = -0.66, S.D. = 0.66</i>						
Between Groups	1	17.91	17.91	34.53	0.001*	1.54
Total	63	32.67	0.52			

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40) and healthy volunteers (N = 25). *df* = degrees of freedom. *SS* = sum of squares. *MS* = mean square. * $p < .001$

Figure 6. *Group Differences on Psychosocial Stress Measures*



4.3.3 Exploratory Analyses: Group Differences on Resting Biological Stress Measures

Given that results associated with Aim #1 of this research did not fully support the hypotheses that adults with ASD would experience significantly greater cardiovascular reactivity (Hypothesis 1a) and cortisol reactivity (Hypothesis 2a) than healthy volunteers, a series of exploratory analyses was conducted in order to test whether these two groups differed on resting (pre-stress condition) biological stress measures. While this research question is not associated with a primary hypothesis of this research, it is important to know whether adults with ASD differ from healthy volunteers in terms of their resting biological stress response even if their patterns of reactivity to stress are similar. These exploratory analyses included a series of one-way ANOVA tests for resting SBP, resting DBP, resting HR, and resting cortisol. For cardiovascular measures, mean resting values were calculated using the average of the rest period for SBP, DBP, or HR measures. Findings of these exploratory analyses indicated that adults with ASD experienced significantly greater resting HR, $F(1, 63) = 7.54, p = .008$. No significant differences between groups existed for resting SBP, $F(1, 63) = .05, p = .833$, resting DBP, $F(1, 63) = .50, p = .484$, or resting cortisol $F(1, 63) = .23, p = .632$.

4.3.4 Summary of Results for Aim #1

Results of analyses associated with Aim #1 indicated that adults with ASD experienced significantly more SBP reactivity and than did healthy volunteers but did not differ significantly from healthy volunteers in their DBP reactivity, HR reactivity, or cortisol reactivity. On average, participants with ASD exhibited SBP reactivity 0.21 (SD = 0.84) standard deviations above the combined sample mean while healthy volunteers experienced SBP reactivity 0.34 (SD = 1.16)

standard deviations below the combined sample mean – an effect size (Cohen’s d) of 0.54, which is a medium-sized effect (Cohen, 1988). An examination of the scatter cloud of SBP, DBP, HR, and cortisol reactivity confirmed that both the magnitude and distribution of reactivity patterns between adults with ASD and healthy volunteers were remarkably similar, even though significant group differences in SBP reactivity were identified.

Additionally, adults with ASD reported significantly higher psychosocial stress than healthy volunteers. More specifically, they reported greater perceived stress ($M = 19.45$, $SD = 6.68$) than did healthy volunteers ($M = 11.40$, $SD = 6.37$) and more stressful life events ($M = 118.00$, $SD = 31.14$) than did healthy volunteers ($M = 81.28$, $SD = 22.95$), leading to a psychosocial stress composite score that was, on average, 0.42 ($SD = 0.66$) standard deviations above the combined sample mean for participants with ASD and 0.66 ($SD = 0.75$) standard deviations below the combined sample mean for healthy volunteers. The effect sizes (Cohen’s d) for perceived stress, stressful life events, and the psychosocial stress composite were 1.23, 1.34, and 1.54, respectively. These large-sized effects (Cohen, 1988) indicate that adults with ASD report markedly more psychosocial stress than do healthy volunteers.

Post-hoc exploratory analyses were conducted in order to examine group differences in resting stress biomarkers; they revealed that adults with ASD had a significantly higher resting HR (ASD: $M = 83.28$, $SD = 15.62$ | healthy volunteer: $M = 73.60$, $SD = 10.25$) than did healthy volunteers (representing an effect size of $d = 0.73$, a large-sized effect; Cohen, 1988) but did not differ from healthy volunteers on resting SBP (ASD: $M = 115.54$, $SD = 10.59$ | healthy volunteer: $M = 117.79$, $SD = 13.65$), resting DBP (ASD: $M = 67.36$, $SD = 9.17$ | healthy volunteer: $M = 68.36$, $SD = 11.25$), or resting cortisol (ASD: $M = 14.59$, $SD = 7.87$ | healthy volunteer: $M = 15.74$, $SD = 11.34$). Based on these findings, the hypothesis that adults with ASD

would experience greater cardiovascular reactivity (Hypothesis 1a) than healthy volunteers was only partially supported, the hypothesis that adults with ASD would experience significantly greater cortisol reactivity (Hypothesis 1b) than healthy volunteers was unsupported, and the hypothesis that adults with ASD would report more psychosocial stress (Hypothesis 1c) than healthy volunteers was fully supported.

4.4 AIM #2: EXAMINE THE RELATIONSHIP BETWEEN STRESS RESPONSE AND SOCIAL OUTCOMES IN ADULTS WITH ASD

4.4.1 Bivariate Relationship between Stress Response and Social Functioning in Adults with ASD

Analyses associated with Aim #1 revealed that adults with ASD experience significantly greater SBP reactivity, resting HR, and psychosocial stress than healthy volunteers. Next, in order to address Aim #2, the relationship between stress and social functioning in adults with ASD was examined. The first step to investigating this aim was to examine the bivariate relationships between the stress measures and the social functioning composite measure. This examination included five separate analyses to assess the relationship between the social functioning composite score and the four biological stress response scores (SBP reactivity, DBP reactivity, HR reactivity, cortisol reactivity), as well as the psychosocial stress composite. As noted in Table 16, there was not a significant association between any of the biological stress response measures or the psychosocial stress composite and the social functioning composite. These findings surprisingly suggest little or no association between biological stress response

and social functioning or between psychosocial stress and social functioning. Thus, based on these results, the hypotheses that a significant negative relationship between cardiovascular reactivity and social functioning (Hypothesis 2a), cortisol reactivity and social functioning (Hypothesis 2b), or psychosocial stress and social functioning (Hypothesis 2c) were unsupported.

Table 16. *Correlations between Stress Response Measures and Social Functioning Composite*

Variable	Social Functioning
SBP reactivity	0.22
DBP reactivity	-0.02
HR reactivity	-0.08
Cortisol reactivity	0.10
Psychosocial Stress	-0.23

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40). SBP = systolic blood pressure. DBP = diastolic blood pressure. HR = heart rate.

4.4.2 Exploratory Analyses: Relationship between Stress Response and Social Functioning Variables, Adjusting for Treatment Exposure, in Adults with ASD

After the associations between biological stress response measures and the psychosocial stress composite and the social functioning composite were tested, a series of exploratory analyses was conducted in order to test the associations between all stress variables and all social functioning variables. Stress variables included SBP reactivity, DBP reactivity, HR reactivity, cortisol reactivity, PSS, and SSS. Social functioning variables included the SAS-II, GAS, and SRS. As noted in Table 17, these exploratory analyses revealed significant, positive associations between the PSS and the SAS-II ($r = 0.47, p = 0.023$) and the SSS and the SAS-II ($r = 0.45, p = 0.038$). Thus, there is a significant, positive association between perceived stress and social

disability such that greater perceived stress is associated with greater social disability. There is also a significant, positive association between stressful life events and social disability, such that experiencing a larger number of stressful life events is associated with greater social disability.

Table 17. *Correlations between Stress Response Measures and Social Functioning Measures*

Variable	SAS-II	GAS	SRS
SBP reactivity	-0.23	-0.04	-0.22
DBP reactivity	0.17	0.10	-0.03
HR reactivity	0.09	-0.03	0.05
Cortisol reactivity	-0.04	0.19	0.02
PSS	0.47**	0.05	0.00
SSS	0.45**	-0.09	-0.10

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40). SBP = systolic blood pressure. DBP = diastolic blood pressure. HR = heart rate. PSS = Perceived Stress Scale. SSS = Stress Survey Schedule. SAS-II = Social Adjustment Scale-II. GAS = Global Assessment Scale. SRS = Social Responsiveness Scale.

* $p < .05$; ** $p < .01$

Having found that significant associations existed between the PSS and the SAS-II and the SSS and the SAS-II, a series of hierarchical multiple regression analyses was run in order to test the association between these variables, controlling for treatment exposure. The results of these analyses are detailed in Table 18 and Figure 7. As noted below, all bivariate associations held at the multivariate level, when controlling for treatment exposure, indicating that greater perceived stress and more stressful life events both predict social disability, when controlling for treatment exposure, in adults with ASD.

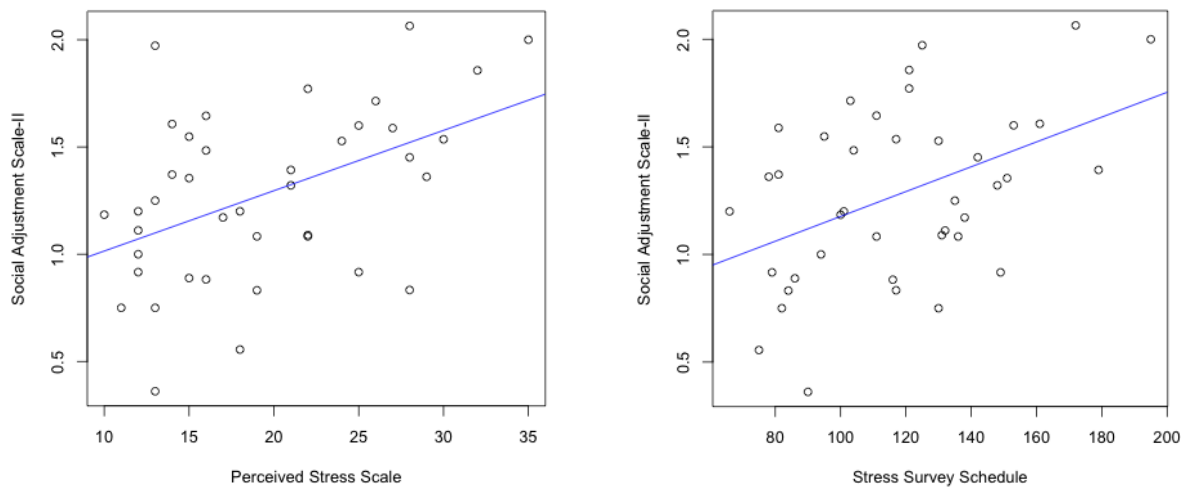
Table 18. *The Relationship between Stress Response and Social Functioning, Adjusting for Treatment Exposure, in Adults with ASD*

Variable/Step	B	SE	β	t	p
<i>PSS and SAS-II</i>					
Step 1					
Treatment Exposure	0.006	0.014	0.071	0.441	0.661
Step 2 ($\Delta R^2 = .22^{**}$)					
PSS	0.072	0.023	0.484	3.217	0.003**
<i>SSS and SAS-II</i>					
Step 1					
Treatment Exposure	0.006	0.014	0.071	0.441	0.661
Step 2 ($\Delta R^2 = .20^{**}$)					
SSS	0.015	0.005	0.452	3.001	0.005**

Note. Analyses conducted on the sample of treatment-exposed adults with ASD (N = 40). SRS = Social Responsiveness Scale. PSS = Perceived Stress Scale. SSS = Stress Survey Schedule. SAS-II = Social Adjustment Scale-II.

* $p < .05$, ** $p < .01$

Figure 7. *Associations between Stress Response and Social Functioning in Adults with ASD*



4.4.3 Summary of Results for Aim #2

Results of analyses associated with Aim #2 revealed no significant associations between SBP reactivity, DBP reactivity, HR reactivity, cortisol reactivity, or psychosocial stress and social functioning in adults with ASD. As such, the hypotheses that there would be a significant relationship between stress response and social functioning in adults with ASD such that greater cardiovascular reactivity (Hypothesis 2a), greater cortisol reactivity (Hypothesis 2b), and more self-reported psychosocial stress (Hypothesis 2c) would predict poorer social functioning were unsupported by this research. Exploratory analyses that examined the associations between components of stress response and social functioning measures revealed moderate to large sized associations between perceived stress and social disability and stressful life events and social disability – components of psychosocial stress and social functioning – when controlling for treatment exposure. Thus, there is a significant, positive association between perceived stress and social disability such that greater perceived stress is associated with greater social disability. Findings also indicated that there is a significant, positive association between stressful life events and social disability, such that more stressful life events are associated with greater social disability. These analyses did not reveal significant associations between stress biomarkers and social functioning measures or between psychosocial stress measures and global functioning or social impairment.

5.0 DISCUSSION

Persistent problems with social functioning are both diagnostic of ASD and problematic for affected individuals throughout the life course (Gillespie-Lynch et al., 2012; Klin et al., 2007; Shattuck, Narendorf, et al., 2012; Smith et al., 2012; Taylor & Seltzer, 2011; Wing & Gould, 1979). Yet, research has revealed few modifiable predictors of social functioning in adults with ASD that can be targeted with focused treatment. The noted challenges with social functioning, coupled with the biobehavioral vulnerabilities inherent to ASD (Chamberlain & Herman, 1990; Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Hill et al., 1977; Jansen et al., 2003), place affected individuals at increased risk for psychophysiological distress (Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Lanni et al., 2012; Levine et al., 2011; Spratt et al., 2012). Effective stress management is essential to optimal adjustment in adulthood (Cohen, Kamarck, & Mermelstein, 1983; Cohen & Williamson, 1988; 1991; Selye, 1956; Williams, 2008). Stress likely factors heavily into both daily life and long-term outcomes for adults with ASD, as suggested by a growing literature that indicates that children with ASD respond physiologically differently, and possibly in a heightened manner, to distress and that adults with ASD may experience greater perceived stress and report more stressful life events than healthy volunteers (Bishop-Fitzpatrick et al., 2015; Corbett et al., 2006; Corbett et al., 2008; Corbett et al., 2009; Groden et al., 2001; Hirvikoski & Blomqvist, 2015; Lanni et al., 2012; Levine et al., 2011; Spratt et al., 2012). However, research to date has not examined the

combined impact of biological stress response and psychosocial stress in adults with ASD or their interrelation. Research has also not examined whether biological stress response and psychosocial stress predict social functioning in this population.

This research sought to examine the role of stress in social functioning in adults with ASD by: (1) comparing both biological stress response and psychosocial stress in adults with ASD and healthy volunteers; and (2) examining the relationship between biological stress response and psychosocial stress and social functioning in adults with ASD. A combination of primary data collected for the purpose of this research and secondary data from an ongoing randomized clinical trial of CET and EST for adults with ASD were used to (1) identify differences in stress response among treatment-exposed adults with ASD and healthy volunteers, and (2) examine the relationship between stress response and social outcomes in adults with ASD. This chapter will provide an overview of the results of this study, as well as a discussion of its limitations and its implications for research and social work practice.

5.1 SUMMARY OF FINDINGS

This research advances knowledge about stress and modifiable predictors of adult outcomes in ASD in two main ways. First, this research found that adults with ASD and healthy volunteers exhibit remarkably similar patterns of biological stress response, yet the ASD group reported more psychosocial stress than healthy volunteers. More specifically, adults with ASD exhibited markedly greater psychosocial stress and slightly greater SBP reactivity than did healthy volunteers, yet the two groups exhibited no significant differences in DBP reactivity, HR reactivity, or cortisol reactivity. These findings emerged despite clear evidence that the Social

Stress Recall Task elicited statistically significant changes in biological stress response and the fact that significantly fewer adults with ASD than healthy volunteers were employed, lived independently, or had completed higher education. This represents a pattern of increased psychosocial stress despite less interaction with situations and experiences such as those that could create stress in adults with ASD.

The second major finding of this research was that psychosocial stress was a pertinent predictor of social disability in adults with ASD, but that biological stress response did not predict social functioning in the group. More specifically, individuals who reported greater perceived stress and more stressful life events experienced greater social disability, which persisted after controlling for treatment exposure. This finding indicates that perception of life as distressing and stressful predicts social disability in this population while measured biological response to stress does not.

The broader implications of these two main findings will be discussed below in greater detail within the context of the specific aims of this research. Then, this section will proceed with a discussion of the limitations of this study and suggestions for future research to verify and confirm the conclusions reached herein. A detailed discussion of the findings of this research follows.

5.1.1 Stress Differences in Adults with ASD and Healthy Volunteers

The first aim of this research was to identify differences in stress (both biological stress response and psychosocial stress) among treatment-exposed adults with ASD and healthy volunteers by: (1) examining cortisol reactivity and cardiovascular reactivity during both a stressor and rest condition in a social stress challenge task; and (2) examining self-reported

psychosocial stress. As noted previously, little is known about differences between adults with ASD and healthy volunteers in terms of cardiovascular reactivity, cortisol reactivity, and psychosocial stress, although preliminary work in children with ASD indicates that, while children with ASD respond differently to stress than do healthy volunteers, no consistent response pattern exists although many studies indicate heightened reactivity (Corbett et al., 2008; Corbett et al., 2009; Goodwin, Groden, Velicer, & Diller, 2007; Groden et al., 2005; Hollocks, Howlin, et al., 2014; Lanni et al., 2012; Levine et al., 2011; Spratt et al., 2012). Additionally, preliminary work on psychosocial stress indicates that adults with ASD report greater perceived stress and more stressful life events than do healthy volunteers (Bishop-Fitzpatrick et al., 2015; Groden et al., 2001; Hirvikoski & Blomqvist, 2015). Because of these previous findings, this research hypothesized that adults with ASD would have greater cortisol reactivity (Hypothesis 1a) and cardiovascular reactivity (Hypothesis 1b) and experience more psychosocial stress (Hypothesis 1c) than healthy volunteers.

Surprisingly, findings indicate that adults with ASD experienced greater SBP reactivity than healthy volunteers but did not differ from healthy volunteers in their DBP reactivity, HR reactivity, or cortisol reactivity. An examination of the scatter cloud of SBP, DBP, HR, and cortisol reactivity confirmed that both the magnitude and distribution of reactivity patterns between adults with ASD and healthy volunteers were remarkably similar, even though significant group differences in SBP reactivity were identified. These results suggest more similarity than difference in patterns of biological stress response between adults with ASD and healthy volunteers, which is contrary to findings that children with ASD experience greater cortisol reactivity and cardiovascular reactivity than healthy volunteers (Schupp et al., 2013; Spratt et al., 2012).

As expected, and contrary to the present research's findings related to biological stress response, adults with ASD reported significantly higher psychosocial stress than healthy volunteers. More specifically, they reported greater perceived stress than did healthy volunteers and more stressful life events than did healthy volunteers, leading to a significantly greater psychosocial stress composite score. The effect sizes (Cohen's *d*) for perceived stress, stressful life events, and the psychosocial stress composite were large-sized effects (Cohen, 1988), indicating that adults with ASD report markedly more psychosocial stress than do healthy volunteers.

Post-hoc exploratory analyses were conducted in order to examine group differences in resting stress biomarkers; they revealed that adults with ASD had a significantly higher resting HR than did healthy volunteers (a large-sized effect; Cohen, 1988) but did not differ from healthy volunteers on resting SBP, resting DBP, or resting cortisol. These exploratory analyses once again emphasize the lack of difference between the ASD and healthy volunteer groups on stress biomarkers. At first glance, these findings violate common sense impressions about biomarkers and a body of research that confirms the association between psychosocial stress and biological stress response in healthy individuals and children with autism (Cohen et al., 2000; De Vente, Olf, Van Amsterdam, Kamphuis, & Emmelkamp, 2003; Goodwin et al., 2006; Groden et al., 2005). However, new findings in ASD research help to bridge the gap and reconcile these two seemingly contradictory results in the present study. Specifically, these new findings indicate that biological stress response differences between children with ASD and healthy volunteers may be relegated to lower-functioning children with ASD (Putnam, Lopata, Thomeer, Volker, & Rodgers, 2015). Further, a large body of research exists describing the phenomenon of burnout and its impact on biomarkers over the course of the lifespan (e.g., Juster, McEwen, &

Lupien, 2010; Kasuya, Polgar-Bailey, & Takeuchi, 2000; Weber & Jaekel-Reinhard, 2000; Williams, 2008).

Newly-released findings indicate that, in terms of cortisol levels and cortisol reactivity, children with ASD and with substantial cognitive impairment (mean IQ = 48.09) differ significantly from children with ASD without cognitive impairment (mean IQ = 105.78) and healthy volunteers (mean IQ = 111.69), but that children with ASD and without cognitive impairment do not differ from healthy volunteers (Putnam et al., 2015). Thus, differences in resting cortisol and cortisol reactivity between children with ASD and healthy volunteers may be a phenomenon specific to lower-functioning individuals with ASD. However, it must be emphasized that the findings of the current research indicate that higher-functioning adults with ASD experience a great deal of psychosocial stress despite exhibiting similar patterns of biological stress response to healthy volunteers. Thus, for higher-functioning adults with ASD, it may be that perception of stress, and not actual biological response to stress, drives group differences.

A second possible explanation is that adults with ASD experience hypothalamic-pituitary-adrenal axis and sympathetic-adrenal-medullary axis burnout due to chronic stress. Burnout, or burnout syndrome, which is often associated with chronic occupational stress or family caregiving, is generally characterized by exhaustion, alienation from activities, and reduced performance (e.g., Kasuya et al., 2000; Weber & Jaekel-Reinhard, 2000) and is associated with increased allostatic load (Juster et al., 2010; Williams, 2008). In general, burnout patients exhibit a pattern of blunted biological response to stress despite reporting high levels of psychosocial stress. More specifically, this takes the form of similar cardiovascular and cortisol reactivity patterns and resting blood pressure and cortisol to healthy volunteers, yet heightened

resting heart rate (De Vente et al., 2003). This is the pattern that was found in this research on stress in adults with ASD, suggesting that adults with ASD may have a blunted biological response to psychosocial stress because of chronic, ongoing stress. A pattern of chronic stress and heightened biological stress response has been identified relatively consistently in children with ASD (Cohen et al., 2000; De Vente et al., 2003; Goodwin et al., 2006; Groden et al., 2005), and this very pattern may lead to HPA axis and SAM axis burnout, or a blunted biological response to stress, in adults with ASD. This possible explanation is also supported both by the lack of association between biological stress measures and the lack of association between biological stress response and psychosocial stress measures, which is also consistent with burnout (De Vente et al., 2003).

5.1.2 The Relationship between Stress and Social Functioning in ASD

While identifying stress response differences between adults with ASD and healthy volunteers was a key aim of this study, the other primary focus of this research was to characterize the relationship between biological stress response and psychosocial stress and social functioning in adults with ASD. Analyses conducted in order to address this aim hypothesized that there would be a significant relationship between stress and social functioning in adults with ASD such that greater cardiovascular reactivity (Hypothesis 2a), greater cortisol reactivity (Hypothesis 2b), and more self-reported psychosocial stress (Hypothesis 2c) would predict poorer social functioning. These hypotheses were not supported by the main analyses of this research. Rather, the relationship between stress and social functioning was more nuanced than predicted.

Exploratory analyses that examined the associations between components of stress and social functioning measures revealed moderate to large sized relationships (Cohen, 1988) between perceived stress and social disability, and stressful life events and social disability, after controlling for treatment exposure. These analyses did not reveal significant associations between biological stress response and social functioning measures or between psychosocial stress measures and global functioning or social impairment. While it was hypothesized that psychosocial stress would predict social disability, biological stress response did not predict social functioning and psychosocial stress did not predict either global functioning or social impairment. However, these findings suggest that, as with findings detailed above on stress differences between adults with ASD and healthy volunteers, perception of stress in day-to-day life is important and likely drives the association between stress and social functioning such that perceiving life as stressful, rather than experiencing a strong biological response to stress, predicts social functioning in this population.

Several factors could explain the disparate associations between biological stress response and psychosocial stress and social functioning measures. First, it is possible that, while a significant relationship between psychosocial stress and components of social functioning was identified in this research and previous preliminary research (Bishop-Fitzpatrick et al., 2015); social functioning in adults with ASD may instead or in addition be predicted by factors other than psychosocial stress. It is certainly possible that stress may not be intrinsically related to social functioning in adults with ASD and that the finding of this research that both greater perceived stress and more stressful life events predict greater social disability are spurious. However, a potentially more promising explanation is informed by emerging evidence that indicates that an individual with ASD's perception of the extent to which they are socially

impaired, but not the actual extent of their social impairment, predicts depressive symptomatology in adults with ASD (Gotham, Bishop, Brunwasser, & Lord, 2014). In other words, much in the same way that perception drives the relationship between stress and social disability, it is also a primary contributing factor in the emergence of depressive symptomatology in individuals with ASD. Consequently, it is possible to conclude that psychosocial stress functions similarly in that it is the perception of day-to-day life as distressing and stressful, not an individual's biological response to stress, that predicts social disability. This phenomenon may be particularly true in the case of high burnout when the biological stress response system is overloaded and stops reacting to environmental triggers.

While it is likely that social functioning in adults with ASD is determined by many genetic, developmental, environmental, and social factors (e.g., Fombonne, 1999; Klin et al., 2007; Magiati et al., 2014; Neuhaus et al., 2010), it seems plausible that a true association exists between psychosocial stress and social functioning. The sample size employed both in this research and in other preliminary work is modest, yet identifies a similarly medium to large sized relationship between psychosocial stress and social disability. This research also did not find that psychosocial stress predicts global functioning, a finding echoed by preliminary research (Bishop-Fitzpatrick et al., 2015), or autistic social impairment.

Notably, while other factors may predict social functioning, the other known predictors of social functioning in ASD (i.e., IQ and childhood verbal ability; Cederlund et al., 2008; Farley & McMahon, 2014; Farley et al., 2009; Gillespie-Lynch et al., 2012; Howlin et al., 2004; Kobayashi et al., 1992) are not easily modifiable through treatment while psychosocial stress has been shown to be modifiable with targeted stress management interventions in individuals not affected by ASD (Antoni et al., 2001; Campo et al., 2008; Kirby et al., 2006; Williams, 2008;

Williams et al., 2010; Williams, Brenner, Helms, & Williams, 2009). Very few modifiable predictors of social functioning in adults with ASD have been identified to date. The trend-level association between psychosocial stress and treatment exposure in this study that included data from an intervention trial of two treatments that were hypothesized to have a non-trivial impact on, but are not designed to target, stress response (Eack et al., 2013; Hogarty & Greenwald, 2006) lends credence to this assertion. Thus, based on the findings of this research, psychosocial stress is likely to be a modifiable predictor of social functioning in adults with ASD.

In summary, the results of this research suggest that adults with ASD perceive and experience life as more distressing than do healthy volunteers and that this perception predicts greater social disability. As will be discussed in greater detail below, these findings are limited by a number of factors, yet provide promising evidence that psychosocial stress may be a modifiable predictor of social disability in adults with ASD.

5.2 LIMITATIONS

Prior to discussing the implications of this study for future research and social work practice, it is necessary to note a number of limitations that temper the conclusions that can be drawn from this work. While hypotheses were developed based on previous research and preliminary evidence, this research was conceptualized and data collection was begun as this field of research was emerging. The aims investigated in this research hypothesized group differences in stress between adults with ASD and healthy volunteers and a significant prediction of social functioning by stress in adults with ASD, although the extent and degree of group differences or the degree to which stress and social functioning were related remained largely

unknown before commencement of this research. Because of the exploratory nature of this research, and its modest sample size, the analytic approach used was conservative and favored maintaining statistical power by avoiding multiple inference testing in order to reduce type I error (Shaffer, 1995). While individual psychosocial stress and social functioning measures were combined into composites for primary hypotheses in order to reduce the possibility of type I error, biological stress response measures did not meet reliability criteria as a composite and were thus treated individually. In addition, while not used to test the primary hypotheses of this research, a number of post-hoc exploratory analyses were conducted in order to assess for associations among individual variables. These factors lead to the possibility of type I error in this research due to multiple inference testing. Results should thus be interpreted with caution.

In addition to potential issues with multiple inference testing, this research is limited by its modest sample size. Because the relative magnitude of effect was unknown before commencing this research, and because of the exploratory nature of this data collection, power estimates were set to detect medium to large effects and not small or small to medium effects. Thus, adequate power in this research could only detect medium to large effects for all study aims. This limitation is most apparent in the composite associations between SBP reactivity and social functioning ($r = 0.22$, $p = 0.18$) and between psychosocial stress and social functioning that approached marginal significance ($r = -0.23$, $p = 0.16$), as well as the number of non-significant associations between individual stress response and social functioning variables in adults with ASD. However, the specific aims of this research were geared towards identifying a modifiable predictor of social functioning in adults with ASD that can be addressed with targeted treatment in future research. Given that the relationship between a modifiable predictor and social functioning should be sufficiently large in order to develop a targeted treatment that can

substantively improve it (Rosen, Proctor, & Staudt, 2003), this research was concerned primarily with identifying factors that predict a moderate to large amount of variation in social functioning and was thus adequately powered in order to address this specific concern.

Another limitation of this research relates to the sample. This research utilized participants with ASD who were current or former participants in an intervention trial of two treatments for ASD that have been shown in pilot work to lead to improvements in functioning in this population (Eack et al., 2014). The secondary data employed in this research was taken from the timepoint nearest to when primary data were collected for the purpose of this study. Thus, primary data and secondary data were not collected on the same day of testing, although significant associations were found between variables collected on different days of testing (i.e., psychosocial stress measures and social disability). In addition, this trial included only individuals who had IQ scores greater than or equal to 80, who were between the ages of 18 and 45, and who had problems with functioning that warranted some treatment. In addition, selection bias may be an issue since the adults with ASD who participated in this research are probably higher-functioning, have more free time, or have more familial support than non-participants. This is because in order to participate in this current research, individuals had to be high functioning enough to participate in a structured intervention program with substantial cognitive and behavioral components *and* have the available time and support necessary to attend hour-long sessions one or more times per week for 18 months. Thus, the individuals with ASD included in this study are not necessarily representative of the entire spectrum of individuals with ASD and may, in fact, be functioning better overall and have better support than many individuals with an ASD diagnosis. Studying stress and social functioning in this group of individuals with ASD may paint a more cautious picture of differences in stress between

individuals with ASD and healthy volunteers and the relationship between stress and social functioning in adults with ASD than would necessarily be found in the entire very heterogeneous population of adults with ASD. In fact, there may be a stronger and less nuanced relationship between stress and social functioning at the low end of the spectrum and not the high end (Putnam et al., 2015) because individuals at the low end are more likely to engage marked repetitive behaviors (e.g., hand flapping, echolalia), which have been associated independently with both poor social functioning and heightened stress in ASD (e.g., Bishop, Richler, & Lord, 2006; Farley & McMahon, 2014; Lewis & Bodfish, 1998).

Another limitation is related to collection of data for this study. Measures included self-report measures, parent-report measures, clinician-rated measures, and biological measures. All of these types of measures have disadvantages. The biological measures used in this research may have created difficulties with sensory input in individuals with ASD given that they involved pressure (blood pressure and heart rate) and taste (Salivettes for cortisol samples) that in some cases were unpleasant for participants. Necessary discussions with participants who were uncomfortable with either the blood pressure cuff or the salivettes before testing may have made participants more comfortable with participating in this research, thus blunting the potential stress response found. This may have biased findings. In addition, all measures that include some form of self-report (i.e., self-report, parent-report, clinical interview) engender validity issues related to social desirability bias that may lead individuals to provide socially desirable answers to paper and pencil or clinician-posed questions (Fisher, 1993). In ASD research, this may work differently for individuals with ASD, who may be more honest (Scheeren, Begeer, Banerjee, Terwogt, & Koot, 2010), or their parents, who may respond that their children are more impaired because it is more socially desirable (Myers, Mackintosh, &

Goin-Kochel, 2009). In addition, this research was explicitly stated to be about stress in individuals with autism during recruitment and in consent forms. Because of this, it is possible that individuals with autism were primed to report higher stress because doing so would be the socially desirable thing to do. In ASD, self-report measures are thought to have disorder-specific drawbacks: research generally indicates that individuals with ASD have a more favorable impression of themselves and their abilities than their parents do, possibly indicating that these individuals underestimate the extent of their difficulties (Johnson, Filliter, & Murphy, 2009; Lerner, Calhoun, Mikami, & De Los Reyes, 2012). However, higher-functioning adolescents and adults with ASD do report poorer social competency than healthy volunteers (Williamson, Craig, & Slinger, 2008) and exhibit a relatively high degree of self-awareness (Vuletic, 2010). Thus, in lower-functioning individuals with ASD, self-report measures should be interpreted with caution, but this caution may not be necessary in individuals who are higher functioning (like those who participated in this study) because of their relatively high degree of self-awareness. These issues with self-report measures could bias findings about psychosocial stress (both psychosocial stress measures were self-report measures) in Aim #1 and Aim #2.

A number of potential confounders could not be controlled for in this research because no validated measures that target these constructs currently exist. First, adults with ASD receive different types and amounts of treatment and services as adults, and also received differential amounts and types of treatments and services as children, especially due to age-related cohort effects (Shattuck et al., 2011). Given that autism is a developmental disorder that categorically and necessarily affects development throughout the life course, input throughout the life course from treatments and services will likely impact the course of development and may lead to multiple treatment interference. Beyond this, another potential confounder is the involvement, or

lack thereof, of parents, relatives, and family friends, which could similarly alter the course of development and/or overall social functioning or stress response in these individuals (Greenberg, Seltzer, Krauss, Chou, & Hong, 2004; Orsmond, Seltzer, Greenberg, & Krauss, 2006).

Finally, there is the possibility of a time-order limitation to this research. Although the hypotheses of this research framed higher stress as a predictor of poorer social functioning in ASD, the design of this study precluded a test of directionality, it is likely that a bi-directional relationship exists. More specifically, the social functioning deficits inherent in ASD may lead to adults with ASD experiencing greater stress. It is also possible that, because social situations create less stress when one functions better in them, individuals with better overall social functioning experience less stress. Additionally, it is likely that stress has an additive effect on social impairments such that greater stress leads to greater social impairment, which in turn creates even greater stress.

5.3 IMPLICATIONS

5.3.1 Implications for Research

The results reported herein have a number of important implications for future research, despite the previously noted limitations of this study. This research, as well as previous preliminary work, suggests that adults with ASD experience more psychosocial stress than healthy volunteers. While this result should be studied using larger sample sizes and longitudinally in order to confirm effects, the body of research is highly suggestive that heightened psychosocial stress is a problem in ASD (Bishop-Fitzpatrick et al., 2015; Hirvikoski

& Blomqvist, 2015) and may be associated with poorer social functioning. Although heightened psychosocial stress may be a modifiable predictor of poor social functioning in ASD, more work is needed in this area to determine if adults with ASD across the spectrum respond biologically differently to distress than healthy volunteers.

The results reported herein suggest, a trend towards adults with ASD having a higher resting heart rate and greater SBP reactivity than healthy volunteers. Results do not suggest a trend towards greater DBP reactivity, HR reactivity, cortisol reactivity, resting SBP, resting DBP, or resting cortisol. Given the relative lack of group differences in cardiovascular reactivity and cortisol reactivity found in this research, future research should consider the possibility of examining different biomarkers of chronic oxidative stress, such as heightened plasma malondialdehyde, a measure of cell damage from lipid peroxidation (Nielsen, Mikkelsen, Nielsen, Andersen, & Grandjean, 1997), heightened 8-hydroxy-2'-deoxyguanosine, a cause of free radical-induced oxidative lesions (Valavanidis, Vlachogianni, & Fiotakis, 2009) or telomere shortening, a measure of DNA breakdown and accelerated aging (Houben, Moonen, van Schooten, & Hageman, 2008). In addition, fMRI studies that target differences in the hippocampus, amygdala, insula, and prefrontal cortex might shed light on stress appraisal differences in adults with ASD and healthy volunteers (McEwen, 2007). Better understanding the interplay of biomarkers of chronic, oxidative stress and psychosocial stress in adults with ASD would lead to clearer knowledge whether interventions should specifically target biological stress response systems or if psychosocial interventions that decrease perceived stress and stressful life events are more warranted. Further research on stress biomarkers throughout the life course could also lead to more concrete hypotheses about when interventions that target stress

response in some way would be most effective, whether at some point during childhood, in adolescence, or in adulthood.

Findings of this research suggest that adults with ASD may be experiencing burnout from chronic stress based on their pattern of biological and psychosocial response to stress. Thus, while individuals with ASD may have a heightened biological response to stress as children, chronic stress over the life course leads to the failure of the biological stress response system to function effectively in adulthood. These findings underscore the need to intervene to reduce stress in individuals with ASD early in life, and suggest that interventions that improve stress management and coping skills in childhood or adolescence may be particularly effective, especially if their effective maintenance is reinforced when typical life demands change during the period of transition from adolescence to adulthood. These findings also underscore the need to assist midlife and older adults with ASD to effectively manage conditions that may arise from chronic, oxidative stress. Although not appropriate to address the primary aims of this research, it is possible that findings would be different had cortisol been measured in terms of diurnal rhythm (rhythm of cortisol change throughout the day) or cortisol awakening response (changes in cortisol during the first 30 minutes upon awakening), both measures of stress response, but not of reactivity to acute stressors. In fact, in burnout patients, cortisol awakening response is elevated (De Vente et al., 2003) and thus might be observed in adults with ASD who exhibit other patterns consistent with burnout that were found in this research. In addition, burnout should be specifically assessed using a standardized burnout inventory such as the Maslach Burnout Inventory (Maslach & Jackson, 1981). Studying burnout in this way in an adequately powered sample able to detect small to medium sized effects would be able to confirm whether adults with ASD experience burnout.

Of great interest and importance in the field of autism research is the development and testing of psychosocial interventions in adults with ASD (Bishop-Fitzpatrick et al., 2013; Gerhardt & Lainer, 2011; LeBlanc et al., 2008; Levy & Perry, 2011). However, the development of these interventions has been limited by a lack of knowledge about modifiable predictors of social functioning identified by extant research. Because this research identified psychosocial stress, which may be a modifiable predictor of social disability in adults with ASD, it warrants the development of an intervention that targets perceived stress and stressful life events. This research indicates that individuals with ASD may perceive and experience life stressors differently than individuals who have not been diagnosed with ASD. However, the majority of intervention research conducted on individuals with ASD has concentrated on helping people learn how to behave in rehearsed situations and not on helping them learn skills to process sensory information and handle stress more effectively (Bishop-Fitzpatrick et al., 2013).

Interventions that teach generalizable skills to help people with ASD better process sensory information and handle stress have the potential to create more durable change because their effects can be applied to a wide and varied set of situations and not simply a prescribed set of rehearsed situations. Future research should also consider adapting an existing intervention, especially one that is systematic in nature, which has been tested in individuals not affected by ASD such as the Williams LifeSkills program (Campo et al., 2008; Kirby et al., 2006; Williams et al., 2010; Williams et al., 2009). Furthermore, research on interventions for adults with ASD indicates that interventions which are computer-based can be extremely effective in teaching new skills (Bölte et al., 2002; Faja et al., 2012; Gantman, Kapp, Orenski, & Laugeson, 2012; Golan & Baron-Cohen, 2006; Trepagnier, Olsen, Boteler, & Bell, 2011), and thus a newly developed

intervention program should combine computer-based instruction with clinical supervision and feedback.

In summary, the results of this study provide a number of promising directions for future research, including investigating additional biomarkers of oxidative stress in adults with ASD and developing and testing psychosocial interventions designed to target psychosocial stress in this population. With such research, it is hoped that studies that confirm modifiable predictors of social functioning in ASD, such as psychosocial stress, can serve to inform effective psychosocial interventions for this population.

5.3.2 Implications for Social Work Practice

This research raises a number of questions psychosocial stress may be heightened and may predict social functioning in adults with ASD. Some important, yet tentative, implications for social work practice arise from this study.

This research provides three main implications for social work practice. First, adults with ASD experience life as stressful, and this may limit their full inclusion into the community and workplace. Second, the perception of life as distressing, rather than actual biological response to stress, predicts social disability in adults with ASD. Finally, adults with ASD may be at increased risk of psychiatric or physical morbidity as a result heightened psychosocial stress. These implications, as well as their potential for change through targeted psychosocial treatment, will be discussed in greater detail below.

Findings of this research indicate that adults with ASD experience significantly greater psychosocial stress than healthy volunteers, and this may limit full inclusion into the workplace and community. Many adults with ASD, including participants in this study, lead lives that lack

the connection to others and to the community and its institutions that are commonplace for many unaffected adults (Carter, Harvey, Taylor, & Gotham, 2013; Farley & McMahon, 2014; Farley et al., 2009; Gray et al., 2014; Howlin et al., 2013; Levy & Perry, 2011; Orsmond et al., 2013; Taylor & Seltzer, 2011). Of the adults with ASD who participated in this research, fewer than 50% were participating in any paid employment, fewer than 25% were college graduates, and fewer than 20% lived independently. This lack of connection may be because adults with ASD choose to avoid situations that might create psychosocial stress. Thus, social workers may be able to assist adults with ASD to engage more fully in the community by helping them to successfully manage their psychosocial stress. However, the possibility exists that fuller inclusion into the community and the workplace could create more stress for many adults with ASD. Thus, any efforts to improve inclusion should be coupled with efforts to manage the potential for heightened stress that may result from increased social and community engagement.

This research indicates that perception of life as distressing, rather than one's actual biological response to stress, both differentiates adults with ASD from healthy volunteers and predicts social disability in adults with ASD. While this finding was surprising, it aligns with emerging research that suggests that perceived social impairment, but not necessarily actual impairment, may predict depressive symptomatology (Gotham et al., 2014), thus suggesting that an individual with ASD's own perception of their abilities to handle life's challenges plays a key role in predicting functioning. While the literature on individuals who are unaffected by ASD does consistently find that individual differences in management of stress and emotion play a central role in predicting overall social functioning (Eisenberg et al., 2000; Kessler et al., 1985), this literature consistently finds a similar relationship between biological stress response and social functioning and psychosocial stress and social functioning (Eisenberg & Fabes, 1992;

Kessler et al., 1985; Pulkkinen, 1982), which was not found in this research on adults with ASD. This suggests that different stress mechanisms are associated with social functioning in adults with ASD than in healthy volunteers. Specifically, psychosocial stress, and not biological stress response, is the most accurate predictor of social functioning in adults with ASD. This may reflect that adults with ASD do not feel as though they have the necessary resources to cope with life stressors. Given this, social work practitioners should take into account that the perceptions of adults with ASD are particularly meaningful, and in this case more meaningful than biology, to understanding their outcomes.

Finally, adults with ASD may be at increased risk of psychiatric or physical morbidity as a result heightened psychosocial stress. Research on adults who are unaffected by ASD indicates that heightened psychosocial stress is associated with an increased risk of psychiatric morbidity, such as depression, anxiety, and posttraumatic stress disorder (Dewa, Lin, Kooehoorn, & Goldner, 2007; Johnson & Sarason, 1978; McEwen, 2004), and increased risk of physical morbidity, such as cardiovascular disease, diabetes, and slower recovery from illness (Cohen et al., 2000; Cohen & Williamson, 1991; Williams, 2008). Emerging findings in ASD have indicated that adults with ASD are at risk for increased psychiatric comorbidity, especially depression and anxiety (Antoni et al., 2001; Ghaziuddin, Ghaziuddin, & Greden, 2002; Gotham et al., 2014; Hollocks, Jones, et al., 2014; White, Schry, Miyazaki, Ollendick, & Scahill, 2014). Findings reported herein may represent a mechanism via which adults with ASD develop comorbid psychopathology. These findings also suggest that, although no studies currently exist of quality of life or health in older adults with ASD (van Heijst & Geurts, 2014), adults with ASD may be at increased risk of psychiatric and/or physical morbidity as they age.

This research suggests that social functioning may be modifiable in ASD through improving psychosocial stress and provides continued support for psychosocial treatment designed to improve social functioning in adults with ASD. This research found trend-level associations between cortisol reactivity and treatment exposure and between psychosocial stress and treatment exposure, both in a study of two treatments that, while not designed specifically to target stress in adults with ASD, were hypothesized to have a non-trivial impact on stress in these individuals. Thus, it is likely that both psychosocial and biological response to stress can be modified in some way by treatment, particularly by a treatment designed to specifically target stress response that has been validated in other populations. This finding provides substantial support for the development and testing of such a psychosocial intervention, and social workers are uniquely poised to take a leading role in these treatment development and provision efforts.

It must be underscored that social work practitioners and researchers have yet to take on a leading role in autism research and treatment (Bean & Krcek, 2012; Walsh & Corcoran, 2011). However, social workers are equipped to take on such a role given the necessity of interacting with the issue of poor social functioning in adults with ASD on a systems level (Walsh & Corcoran, 2011), taking into consideration issues of both treatment development and implementation in community-based settings. Evaluating treatments and services for adults with ASD should remain central to the role of social workers in addressing this social problem. Still, addressing the issue of poor social functioning in adults with ASD will take much concerted effort from social work researchers and practitioners at all levels, given the degree of work that must be done in treatment development, service provision, and policy formulation. There is additionally, although not specifically supported by this research, a great need for social workers to assist in advocacy efforts for improved treatments and services for adults with ASD, and to

help assist adults with ASD and their families in organizing and advocating for themselves, where possible.

5.4 CONCLUSIONS

This research sought to explore the role of stress in social functioning in adults with ASD by comparing both biological stress response and psychosocial stress in adults with ASD and healthy volunteers and by exploring the relationship between biological stress response and psychosocial stress and social functioning in adults with ASD. Findings indicated that adults with ASD and healthy volunteers had remarkably similar biological response patterns to stress yet reported significantly higher psychosocial stress. In addition, this research identified that perceived stress and stressful life events predict social disability in adults with ASD through exploratory analyses. Tentative evidence also suggests that both biological stress response and psychosocial stress can be modified with treatment. Future research will need to replicate these findings in larger samples and develop targeted stress management interventions for adults with ASD.

This research advances knowledge of stress response and modifiable predictors of social outcomes by providing evidence that perception of life as distressing, rather than one's actual biological response to stress, both differentiates adults with ASD from healthy volunteers and predicts social disability in adults with ASD. It is hoped that these findings will lead to continued progress on the part of social work researchers and practitioners to identify additional modifiable predictors of social functioning in this population and ultimately develop a set of psychosocial

interventions that can improve people's lives by targeting some of the many, heterogeneous problems with social functioning in adults affected by ASD.

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