Defining and Quantifying Severity of Impairment in Autism Spectrum Disorders Across the Lifespan

by

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Dedication

To my family, Steven Brunwasser and Mary Gotham in particular; my friends, Somer Bishop and Kathryn Howell in particular; and my advisor, Catherine Lord; with immense gratitude to each.

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Abstract

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Chair: Catherine Lord

Individuals with autism spectrum disorders (ASD) vary considerably in language level, cognitive ability, symptom severity, as well as comorbid psychopathology and behavioral issues. The first study in this three-paper project suggests preliminary means to stratify this diverse population into more homogeneous subgroups by ASD severity. Autism Diagnostic Observation Schedule (ADOS) scores were standardized within a large sample to approximate an autism severity metric. The resulting metric was less associated with verbal IQ than were ADOS raw totals, and resulted in increased comparability across age- and language-specific modules of this instrument.

In the second study, standardized ADOS scores were used to plot longitudinal trajectories of ASD severity among children and adolescents. Four latent trajectory

classes were identified, including persistent severe and persistent moderate groups, as well as much smaller classes that increased or decreased in ASD severity over time.

Comorbid psychopathology is another way to characterize impairment in the autism spectrum. The third paper in this series posits that better understanding of the mechanisms that cause and/or maintain depressive symptoms in ASD will contribute to the ability to prevent and treat them, therefore providing one way to improve quality of life for these individuals. The objectives of this study were (1) to explore the relationship between insight into one's own core autism symptoms and the level of depressive symptoms as described by the individual and an informant, and (2) to explore the relationship between social motivation, social participation, and level of depressive symptoms. Insight into functional independence impairments significantly predicted higher depression scores on the Beck Depression Inventory in the sample of adolescents and adults with borderline to above average IQ and ASD. This dissertation is thus focused on severity of impairment in autism spectrum disorders, with 'impairment' defined in relation to both autism-specific and comorbid factors.

Chapter I

Introduction

Since its original description by Leo Kanner in 1943, autism has come to be recognized as a neurodevelopmental disorder that manifests in infancy or early childhood and encompasses both delays and deviance in a "triad" of behavioral domains (Wing & Gould, 1979): reciprocal social interaction, communication, and restricted and repetitive behaviors and interests. Autism is the cornerstone of a spectrum of disorders, commonly referred to as autism spectrum disorders (ASD) or pervasive developmental disorders (PDD). This spectrum includes Asperger syndrome (AS) and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS, or atypical autism).[1]

Impairment in social reciprocity is believed to be the central defining characteristic of autism spectrum disorders (Williams White, Koenig, & Scahill, 2007; Carter, Davis, Klin, & Volkmar, 2005). Difficulties in social interaction present in various ways within and across individuals, such as a toddler who does not direct eye contact or a changed facial expression to her parent when something startles her, but looks up briefly in the direction of the noise and continues playing, an adolescent who interjects abruptly during a group conversation to bring up his own interest in videogames, or an adult who makes no response to another's comment about having a

[1] The autism spectrum also includes two very rare disorders, Rett's disorder and Childhood Disintegrative Disorder (CDD). For the purpose of this paper, these disorders will be excluded from further mention because of their low prevalence and lack of representation in the samples described.

terrible day. Delay, impairment in, or absence of communication strategies is also characteristic of autism. These difficulties are evident in both verbal (e.g., late onset of phrase speech, pronoun reversal, stereotyped speech) and nonverbal (e.g., minimal use of gestures) aspects of communication. Restricted, repetitive behaviors and interests (RRBs) comprise the third domain of autism symptomatology. These include repetitive motor mannerisms (e.g., hand flapping), unusual sensory interests (e.g., squinting one's eyes to peer at a wind-up toy), and restricted or unusual topics of interest (e.g., collecting ticket stubs, learning and reciting everything there is to know about the Roman emperor Nero).

Whereas autism was previously believed to occur in approximately 4 children out of 10,000 based on epidemiological studies published in the 1960's, the autism spectrum is thought to have a combined prevalence rate of 50-60 out of 10,000 school-age children (Chakrabarti & Fombonne, 2005). Research initiated by the Center for Disease Control suggested that number was closer to 1 in 150 live births, with the proportion even greater for males as the more commonly affected sex (CDC, 2007). Refinements to diagnostic criteria surely have impacted these increased prevalence rates (Bishop, Whitehouse, Watt, & Line, 2008), and growing ASD prevalence and awareness of the disorders in turn demand greater research attention to the boundaries of and within this spectrum. Indeed, one of the primary issues in ASD diagnosis today is a debate about the clinical and biological validity of distinct categorical disorders within the spectrum.

Just as there is no reliable biological marker for the autism spectrum, differentiating between subtypes on this spectrum also falls under the realm of behavioral phenotyping. Partly art and partly science, this form of assessment often yields different results by lab and by clinician. For this reason, many clinical researchers have proposed

a shift from a categorical approach in ASD diagnosis towards a more dimensional framework (Constantino & Todd, 2005; Gotham, Pickles, & Lord, 2009). Continuous measures of social and communication difficulties as well as restricted and repetitive behaviors could be used to evaluate a child's level of impairment/ competence across different domains. New techniques would be necessary in order to quantify symptoms on a dimensional scale, with the advantageous result that we may be able to develop more meaningful measures of severity. There is currently no well-defined benchmark for "average autism," so it is difficult to classify children with ASD as mild or severe, especially since a child may have very severe symptoms in one domain of behavior and relatively mild symptoms in another. Validating instruments that take a quantitative approach to symptoms across domains could improve our ability to describe different developmental trajectories and responses to treatment, which would in turn further efforts to identify subgroups of children with ASD and to isolate endophenotypes that map onto specific genetic or neurobiological findings.

Studies of monozygotic twin concordance for autism, and of families in which parents have multiple affected children, have established that risk for ASD is influenced by genetic factors (Morrow et al., 2008; Constantino & Todd, 2008). However, the heterogeneity of autism – prompting some researchers to employ the term "autisms" – adds to the challenge of identifying causal factors. Because ASDs are developmental disorders, they both influence and are influenced by developmental levels of the individual, such as language level, "mental age," and chronological age. Unlike Down Syndrome or other common developmental disorders, the autism spectrum encompasses a wide range of cognitive and language abilities: approximately 15% of individuals

remain nonverbal into later childhood and beyond, compared to 40% who are using fluent complex speech at these ages (Lord et al., 2006); up to 60% have nonverbal IQs in the average range while many others with ASD are intellectually disabled (Fombonne, 2005; Tidmarsh & Volkmar, 2003). Thus, individuals with ASD can look quite different from each other: A nonverbal sixteen-year-old who avoids eye contact and spins in circles might share a diagnosis of autism with a hyperactive, verbally fluent four-year-old who seeks out others to talk at length about his interest in maps and state capitols. If ASD indeed results from a variety of causes, as evidence suggests (Morrow et al., 2008), then researchers must wade through this heterogeneity of symptom expression and developmental level in order to collect samples of individuals similar enough to shed light on a specific one or two out of many possible causal factors. If a general sample is collected based on categorical diagnoses alone, this sample will likely be comprised of ASDs of various etiologies, masking robust findings of specific factors.

Using continuous measures of language ability, IQ, or behavior such as aggression or anxiety may well help to stratify research samples into more homogeneous groups. In fact, genetics researchers commonly group samples by age of first words or phrases, savant skills, or compulsive behavior (Hus, Pickles, Cook, Risi, & Lord, 2007). It is important to note, however, that selecting samples based on similarity of these non-ASD-specific factors may lead to findings of gene locations implicated in precisely these non-ASD-specific conditions, such as intellectual disability. Though similar in IQ or language development or savant skills, these samples may mask heterogeneity of ASD-specific symptoms and etiologies. However, the field has no reliable continuous or categorical measure of severity of autism-specific symptoms by which to stratify research

samples. The first study in this three-paper project aims to provide a temporary measure of severity of 'autism' as it is defined by a 'gold-standard' ASD assessment tool, the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000). This was undertaken by standardizing ADOS diagnostic algorithm scores within a large sample to approximate an autism severity metric. Using a dataset of 1415 individuals aged 2-16 years with ASD or nonspectrum diagnoses, an ASD-only subset of 1807 assessments from 1118 individuals were divided into narrow age- and language-cells. Within each cell, severity scores were based on percentiles of raw totals corresponding to each ADOS diagnostic classification. Calibrated severity scores had more uniform distributions across developmental groups and were less influenced by participant demographics than raw totals. They also showed the expected difference in distribution across autism, PDD-NOS, and nonspectrum diagnoses when scores were applied to the NS sample (again, these data were not used in the creation of the metric itself). This metric should be useful in comparing assessments across modules and time, as well as identifying trajectories of autism severity and behavioral phenotypes for clinical, genetic, and neurobiological research. Chapter 2 of this dissertation details the methods and results of this study.

The objective of the second paper in this series was to plot longitudinal trajectories of ASD severity among children and adolescents using the standardized ADOS scores developed in the first study. Unique trajectories may be a preliminary means by which to conceptualize distinct ASD subtypes. In this study, the standardized ADOS severity metric reported in Chapter 2 (Gotham, Pickles, & Lord, 2009) was applied to 1026 cases of data collected longitudinally from 345 clinic referrals and research participants aged 2-15 years with clinical best estimate diagnoses (of autism,

ASD, or nonspectrum disorders), verbal and nonverbal IQ scores, and repeated ADOS assessments. This was an inception cohort of consecutive ASD referrals to state-funded and private university autism clinics, as well as research participants and clinical patients assessed at these clinics at various ages. Standardized scores were fitted for latent classes of severity trajectories with and without covariates. Adaptive behavior and IQ trajectories over time were modeled and patterns of ADOS domain change described within each of the best-fit latent classes. Chapter 3 of this dissertation describes the methods and results of this study in more detail. If replicated, identified classes of autism severity trajectory may contribute to clinical prognostic ability and to subtyping samples for neurobiological and genetic research.

From a genetic and neurobiological standpoint, it is important to identify ASD severity along a dimensional spectrum in order to identify possible etiological factors. One reason that so much time, money, and human effort continues to be expended toward identifying the cause of ASD is that it is very difficult to eradicate social and repetitive behavior symptoms, and virtually impossible to "cure" these disorders. Perhaps with the knowledge of genetic or neurobiological causes, biological interventions can be developed, specific psychosocial factors can be targeted, and preventative measures can be taken. Until that knowledge is available, a practical stance on current intervention should include focus on tractable factors that affect quality of life in individuals with ASD.

The third paper in this dissertation addresses the public health issue of depressive symptoms in adolescents and adults with high-functioning autism spectrum disorders. In many autism spectrum research samples in which co-occurring psychopathology has been

analyzed, depression is present at much higher rates than in the general population (Stewart, Barnard, Pearson, Hasan, & O'Brien, 2006). The purpose of this study is to examine psychosocial mechanisms that may impact the development of depressive symptoms in autism spectrum disorders (ASD). A sample of 46 individuals with ASD, aged 15 – 31, was recruited through local clinics, social groups, job-finding groups, and ongoing research projects; these participants received a standard autism diagnostic assessment including cognitive testing, and completed questionnaires and semi-structured interviews about social support, symptoms of depression and anxiety, and other psychological comorbidities. Using a measure created for this project, participants rated their own ASD-associated behaviors, as did the examiner assessing them; participants also reported on their own current participation in social interaction along with their desired level of participation. These data were used to explore the hypotheses that (1) greater awareness of one's own social impairments is associated with higher levels of depressive symptoms, and (2) a disparity between social motivation and social participation will predict higher levels of depressive symptoms in this population. With adequate study of the social mechanisms of depressive symptoms in ASD, we may find evidence that relatively simple treatments may improve quality of life for individuals with ASD and their families. The fourth chapter of this dissertation reviews findings on depressive symptoms in ASD and describes the methods and results of this study in greater detail.

As a whole, then, this dissertation examines the concept of 'severity' across the lifespan in autism spectrum disorders. Quantifying autism-specific severity in children and adolescents ideally will aid in stratifying research samples for etiological studies of

ASD, as well as providing a clinical tool for assessing change over time. Examining autism-specific severity trajectories similarly may contribute to phenotypic subtyping and reliability of clinical prognosis. In the adolescent and adult ASD population, this project takes a broader view of “severity” in the sense that comorbid psychopathology influences global severity of impairment beyond autism-specific features.

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Chapter II

Standardizing ADOS Scores for a Measure of Severity in Autism Spectrum Disorders

Currently, levels of impairment in children with autism spectrum disorders (ASD) are measured largely in terms of language delay, cognitive functioning, or behavioral issues such as aggression. While these are important factors in overall adaptive functioning, they are not core features of the autism spectrum. Measuring the relative severity of autism-specific features could contribute to our ability to accurately describe ASD phenotypes across samples and across time in clinical and treatment research. An ASD severity metric could be used in categorizing samples based on severity trajectories (see Liang, Tayo, Cai, & Kelemen, 2005; Harold et al., 2009) into more homogeneous groups in genetic and other neurobiological studies; it would also address a need to document severity as part of clinical assessment.

At this point, measures that provide autism severity ratings, such as the Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1986), the Gilliam Autism Rating Scale (GARS; Gilliam, 1995), or the Autism Behavior Checklist (ABC; Krug, Arick, & Almond, 1980), tend to yield scores that are either strongly correlated with IQ or that do not correspond to standard measures of diagnosis (Gilliam, 1995; Volkmar et al., 1988; Spiker, Lotspeich, Dimiceli, Myers, & Risch, 2002; South et al., 2002; Szatmari, Bryson, Boyle, Streiner, & Duku, 2003). The Social Responsiveness Scale (SRS; Constantino et al., 2003) provides a method for quantifying social impairment that

has shown relative independence from participant characteristics such as IQ. SRS scores are based on parent or teacher report, however, and thus a complementary measure of ASD severity that offers the opportunity to take into account the observations of an experienced clinician would be desirable.

For genetic, neuroscience, and intervention research, severity of core autism features often has been estimated using primary phenotyping measures, the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) and the Autism Diagnostic Interview-Revised (ADI-R; Rutter, LeCouteur, & Lord, 2003). While it is true that higher ADI-R and ADOS scores indicate that an individual has a greater number of items representing core deficits and/or greater severity of impairment, scores were not normalized for this purpose and vary in the degree to which they are correlated with both IQ and chronological age. Attempts to indicate severity using ADI-R item scores selected to operationalize ICD-10 criteria for the disorder proved successful in predicting the number of affected relatives of verbal probands, but not for nonverbal probands (Pickles et al., 2000). One limitations of ADI-R scores as a severity metric is that nonverbal children are not scored on roughly 25% of the total ADI-R items, and so communication domain summary scores are restricted by non-random missing data.

The ADOS, a semi-structured autism diagnostic observation, has shown strong predictive validity against best estimate diagnoses (Gotham, Risi, Pickles, & Lord, 2007), making it a common choice among phenotyping measures. In each of four developmental- and language-level dependent modules, a protocol of social presses is administered by a trained examiner, and then behavioral items relevant to ASD are scored on a 4-point scale, with 0 indicating ‘no abnormality of type specified’ and 3 indicating

'moderate to severe abnormality.' Specific items comprise an algorithm for each module; these items are summed and compared to thresholds, which results in a classification of "autism," "autism spectrum disorder," or "nonspectrum."

Because the ADOS has been used to catalogue ASD features in large samples, ADOS raw totals are a common stand-in for a measure of autism severity. This instrument was created for diagnostic purposes, and thus was not specifically designed to facilitate longitudinal and cross-sectional comparison of data. As an individual gains language skills, he or she potentially moves through ADOS modules, making raw scores not directly comparable across time. Additionally, effects of age and language level on domain total and algorithm scores have been observed (Joseph, Tager-Flusberg, & Lord, 2002; de Bildt et al., 2004; Gotham et al., 2007).

In 2007, the original ADOS algorithms were revised in part for the purpose of increasing the comparability across modules 1-3. Algorithms with the same number of items and of similar content across modules were created (Gotham et al., 2007). These revisions resulted in improved specificity of the measure among more impaired populations, while generally maintaining or improving predictive validity among individuals of other developmental levels (e.g., fluent speakers). The algorithm domain structure now includes a Social Affect (SA) and a Restricted, Repetitive Behavior (RRB) domain for each of the five developmentally-based algorithms corresponding to modules 1-3. Comparability of item content and total item number across these algorithms was intended to improve the interpretability of longitudinal comparisons using the measure. Still, items are necessarily developmentally graded across modules, making calibration necessary to compare algorithm totals.

Some effects of participant characteristics still exist within and across ADOS modules as well. Revised algorithm totals met the goal of independence from chronological age and decreased association with verbal IQ, with the exception of Module 1 scores (Gotham et al., 2007). A replication of the algorithm revisions in an independent dataset again found low correlations between raw scores and age, verbal IQ, and nonverbal IQ, though significant associations remained between verbal IQ and Social Affect domain total scores for Module 1 recipients with few or no single words and Module 2 recipients aged 5 or older (Gotham et al., 2008).

True normalization of severity of autism would require a representative population, but to date, population studies have been too small, e.g., Brick Township (Bertrand et al., 2001), have not used the ADOS (Chakrabarti & Fombonne, 2005; CDC, 2007), or have collected samples older than most clinically assessed children (Baird et al, 2006). Acknowledging these limitations, in the present study we elected to standardize ADOS scores using a large "convenience" sample of individuals with ASD. Our goals were to reduce remaining participant demographic effects to the greatest possible degree, and generate standard scores that would approximate a severity metric for the construct of 'autism spectrum' as it is measured on the ADOS. This metric ideally will be useful in (1) allowing comparison of assessments across modules and time; (2) providing a means of assessing the relationship between severity in ASD and verbal and nonverbal IQ; and (3) identifying different trajectories of autism severity independent of verbal IQ both for clinical purposes and for phenotypic subgrouping in genetic and neurobiological research. We hope that calibrated severity scores can then be replicated in smaller

population-based studies and tested for validity in predicting treatment responsiveness and other clinical outcomes in children with ASD.

Our first approach to developing a severity metric was to calibrate ADOS algorithm totals using eight age/language cells chosen on the basis of theoretically-driven expectations for specific age ranges with similar developmental impairments. This would have allowed a 'prefix' on the severity score that indicated age and language level out of the eight possible groups (ranging from young Module 1's with no words to fluent speakers, aged 5-10). Within each cell, raw totals were converted to Z-scores, which were then converted to a 100-point scale. This method yielded calibrated scores that fanned out, with increasing variability of individuals' ADOS totals over time and age. Thus, an alternative approach was chosen in which a greater number of age/language cells were used, and severity scores within each cell were based on the raw total percentiles that corresponded to each of three possible ADOS diagnostic classifications. This method is described in more detail below.

Methods

Participants

Analyses were conducted on data from 1415 individuals, of which 355 individuals with ASD diagnoses had repeated measure data. The final dataset included 2195 assessments, where 'assessment' is defined as contemporaneous ADOS data and a best estimate clinical diagnosis. Autism diagnoses were assigned to 1187 assessments (54% of entire sample); 599 assessments were given diagnoses of non-autism ASD (27% of the sample, including n=12 with Asperger Disorder, n=3 with Childhood Disintegrative Disorder, and n=584 with Pervasive Developmental Disorder, Not Otherwise Specified,

or PDD-NOS), and 409 had non-ASD developmental delays (19%). Contemporaneous verbal IQ data was available for 2007 assessments (91.4% of the entire sample) and nonverbal IQ data for 1989 assessments (91.0%). Please refer to Table 2.1 for a detailed description of the dataset by revised algorithm group.

Chronological ages in the sample ranged from 2 to 16 years (see Table 2.1 for age range by algorithm group). Recipients of ADOS Module 4 (older adolescents and adults with fluent speech) were not included in these analyses because of smaller sample size and the different relevance of age equivalents in adults. Females comprised 22% of the dataset (N=478 assessments). Ethnicities represented by these data include 14% African American (N=306 assessments); 3% Asian American (N=58); 77% Caucasian (N=1699); 0.5% Native American (N=10); 2% biracial (N=40); and other (N=20) or race not specified (N=62) totaling 4% of assessments. Twenty-three percent of the sample reported maternal education at the graduate or professional level; 56% of mothers had a bachelor's degree or some college education, and 21% of mothers had a high school degree or less.

Within the nonspectrum sample of 409 assessments, 111 had a primary diagnosis of a language disorder (27% of nonspectrum total), 80 were assessments with nonspecific intellectual disability (20%), 56 with Down syndrome (14%), 55 with oppositional defiant disorder, ADD and/or ADHD (13%), 31 with mood and/or anxiety disorders (8%), 29 with Fetal Alcohol Spectrum Disorders (7%), 24 with non-ASD genetic and/or physical disabilities such as Fragile X, Williams syndrome, or mild cerebral palsy (6%), and 23 had an early delay that clinicians were not comfortable categorizing (5%).

The majority of participants were self-, school-, or physician-referred clinic patients at the University of Michigan Autism and Communication Disorders Center (UMACC) or the University of Chicago Developmental Disorders Clinic. The rest participated in a longitudinal study conducted through the Treatment and Education of Autistic and Communication Handicapped Children (TEACCH) Centers at the University of North Carolina, Chapel Hill, and the University of Chicago clinic, or received diagnostic evaluations through recent, ongoing studies at UMACC, including those focused on participants with non-ASD developmental delays, ASD-affected sibling pairs, or children between 12 and 36 months of age who failed a social-communication screener. Out of 399 participants with repeated assessments through clinic reevaluations or longitudinal research, 301 individuals had 2 or 3 ADOS assessments (57% with autism, 31% with PDD-NOS, and 12% NS), and 98 individuals had between 4 and 8 assessments (58% with autism, 33% with PDD-NOS, and 9% NS). Individuals with longitudinal data did not differ significantly in gender, race, or maternal education from those with only one assessment point, however they had significantly lower mean verbal IQs (M=49.6, SD=27.8) and nonverbal IQs (M=73.0, SD=23.8) at first assessment than did single assessments (verbal IQ M=68.2, SD=32.8; nonverbal IQ M=77.9, SD=27.5); verbal IQ $t(1351)=9.7$, $p<.001$ and nonverbal IQ $t(1334)=3.0$, $p<.01$.

Measures and Procedure

The most typical research protocol across sites and projects was the initial administration of the ADI-R and the Vineland Adaptive Behavior Scales, 1st (VABS; Sparrow, Balla, & Cicchetti, 1984) or 2nd edition (Vineland II; Sparrow, Cicchetti, & Balla, 2005), to a parent or caregiver, followed by a child evaluation in which

psychometric testing preceded the ADOS. The second most common protocol was a re-evaluation consisting of psychometric testing and an ADOS. In both cases, a clinical diagnosis was made by a psychologist and/or psychiatrist after review of all data. The ADI-R was available for 1700 assessments (77% of sample) and the Vineland for 1710 assessments (78%). The ADOS was administered and scored by a clinical psychologist or trainee who met standard requirements for research reliability. The Pre-Linguistic Autism Diagnostic Observation Schedule (PL-ADOS; DiLavore, Lord, & Rutter, 1995) was given in 418 assessments (19%) and the piloted ADOS-T (Luyster et al., submitted), a toddler version of the ADOS, was given in 82 assessments (4%); for both measures, identical items were recorded to Module 1 algorithm scores. A developmental hierarchy of cognitive measures, most frequently the Mullen Scales of Early Learning (MSEL; Mullen, 1995) and the Differential Ability Scales (DAS; Elliot, 1990), determined IQ scores.

Clinic-referred participants received oral feedback and a written report without financial compensation. Participants recruited only for the purpose of research received financial compensation and a written summary of evaluation results. Institutional Review Boards at the University of Chicago or the University of Michigan approved all procedures related to this project.

Mapping a standardized severity metric onto raw ADOS scores

Severity scores were created by dividing the pool of assessments from individuals with ASD into narrowly defined age and language cells, and standardizing raw total scores from the revised algorithms (Gotham et al., 2007) within these cells. In order to maximize the number of cases available for standardization, assessments missing data

from any one item from either the Social Affect (SA) or Restricted Repetitive Behavior (RRB) domains of the revised ADOS algorithms were retained by adding to the domain total an average item score from that participant's existing domain data. The ASD sample alone was used for raw total standardization: this included all assessments corresponding to a best estimate diagnosis of autism or ASD, as well as data from 13 individuals who had ADOS data with a contemporaneous nonspectrum diagnosis but who were later diagnosed with ASD. This subsample (N=1807 assessments from 1118 individuals) was separated into groups based on the five revised algorithms used with children: Module 1 No Words, Module 1 Some Words, Module 2 Younger than 5; Module 2 Age 5 and Older; and Module 3. Within each of these five developmental cells, distributions of summed Social Affect and Restricted Repetitive Behaviors totals were generated separately for every one-year age group between 2 and 16 years; these age cells were collapsed when possible in order to create the fewest number of age- and language-level-determined 'calibration cells' with similar raw total score distributions. Younger age cells were purposely kept distinct to anticipate developmental changes and more frequent assessments in young children as they transition from toddlerhood to preschool to school programs. Age cells with similar distributions were collapsed only within the same algorithm. Eighteen calibration cells resulted (see Figure 2.1).

Within each of these 18 cells, raw ADOS totals were mapped onto a 10-point severity metric. After considering a variety of approaches, severity scores 1-3 were set so as to represent the distribution of raw scores receiving a nonspectrum ADOS classification within that calibration cell, severity scores 4-5 represented ASD-classification ADOS totals, and 6-10 represented raw totals receiving an autism

classification within that cell. ADOS classification thresholds were determined by the revised algorithm relevant to each calibration cell. The range of raw totals corresponding to each point on the severity metric was determined by the percentiles of available data associated with each severity point within a classification range. Lower severity scores are associated with less autism impairment. Table 2.2 shows the raw score range corresponding to each severity point within each calibration cell.

Design and Analysis

Distributions of raw totals and severity scores were compared to assess whether severity score distributions across age/language cells were more uniform than raw score distributions. Linear regression models were analyzed to compare the relative independence of severity scores and raw totals from participant characteristics, such as chronological age, verbal and nonverbal IQ, and verbal and nonverbal "current" mental ages. Several assessments with longitudinal data were then chosen to exemplify various patterns of severity change over time across diagnostic groups.

Results

Comparing distributions of severity scores and raw ADOS totals by calibration cell

In line with the goal of increasing comparability across modules and developmental levels, severity scores for ASD participants were expected to have a more uniform distribution across age- and language-level calibration cells than would raw totals. Distributions of raw ADOS totals were generated for each of the 18 calibration cells (Figure 2.2) and compared to the distribution of severity scores for each cell (Figure 2.3). Distributions of severity scores showed increased comparability across the

age/language cells, though they were not uniform. The means and standard deviations of both severity scores and raw totals are listed by age/language cell in Table 2.3.

Severity score distributions exhibited a ceiling effect that is inherent to the metric. By ensuring that scores 6-10 correspond to approximate fifths of the ASD participants who received scores in the autism classification range, roughly 20% of participants received the maximum score of '10' (in this dataset, 19.3% of participants with an autism classification on the ADOS have a severity score of '10,' which is 16.5% of all participants). Though some overlap exists, severity scores showed expected heterogeneity of distribution across the three diagnostic groups: autism, PDD-NOS, and nonspectrum (see Figure 2.4).

Relative independence of severity score from participant characteristics

Multiple linear regression analyses were performed separately for the dependent variables *severity score* and *raw total* to examine whether participant characteristics such as age and IQ would be less associated with severity scores than they were with raw scores. For *ASD assessments* with complete contemporaneous demographic data (N=1369), potential predictors were entered into a structured hierarchical model, in which Block 1 included verbal and nonverbal IQ and mental age variables (which are known to affect the expression of ASD symptoms; Lord & Spence, 2006), and Block 2 included age, gender, maternal education, and race (variables that could affect ASD symptoms but that often have had non-significant effects when Block 1 variables are controlled). Whereas 44% of the variance in raw totals was explained by this model, only 12% of variance was explained for severity scores using these covariates. Verbal IQ and one maternal education variable (mothers with graduate/professional degrees versus all

others) emerged as significant predictors for both severity score and raw score. Nonverbal IQ, verbal mental age, nonverbal mental age, chronological age, and gender were not significant predictors of either severity scores or raw totals for ASD participants. When covarying for these variables, as well as verbal IQ and maternal education, there was a trend for African American participants to have lower severity scores than other racial groups combined (B=-.35; β = -.06, p=.04), but this is not easily interpreted due to the confounding effects of possible referral bias. For all ASD assessments with racial affiliation data (N=1749), mean severity score for African-American participants was 7.4 (SD=1.8) compared to 7.3 (SD=2.2) for the combined other participant groups, t(1747)=-.71; p=.48.

Verbal IQ and the graduate/professional maternal education variable were then entered into Forward Stepwise models (see Table 2.4), at which point maternal education was excluded from the model as a predictor of severity score, though retained as a predictor of raw score. Standardization reduced the effect of verbal IQ, the most influential participant characteristic on ADOS scores. Verbal IQ explained 43% of the variance in raw totals in the model, but accounted for only 10% of the variance in severity scores in this model. This represents a change from a large effect size (R=0.67) for verbal IQ on ADOS scores to an effect size just outside the accepted range for 'small' (R=0.32; see McCarthy et al., 1991; Cohen, 1988). The effect of maternal education on raw total scores was likely an artifact of recruitment biases (Graduate/ Professional raw total M=14.9, SD=7.2; other maternal education levels raw total M=15.4, SD=7.2; t(1887)=1.13, p=.26).

When the initial hierarchical block models were applied to the full sample (*ASD and nonspectrum assessments combined*), significant predictors of severity scores included verbal IQ, gender (with males the more severe group), and maternal education; significant predictors of raw totals included verbal IQ, nonverbal mental age, gender, chronological age, and maternal education (these statistics are available from the authors). This again indicates that, when severity scores are applied to a clinical referral population, they are less influenced by participant characteristics than are raw ADOS totals.

Case summaries

Four children with ASD diagnoses and longitudinal data were chosen to exemplify patterns in severity score change over time. Their scores by chronological age are plotted in Figure 2.5, with ADOS module and raw total score displayed for each time point.

Case 1. "Adam," a Caucasian male, was seen at 45 months of age as part of a clinical research project. He received a diagnosis of autism at that time. He was evaluated with ADOS Module 2 until age 13, when he received Module 3. His mental ages were 34 months nonverbal and 21 months verbal at first assessment, and 165 months nonverbal and 111 months verbal at final assessment at age 13 (NVIQ: 71 at first, 107 at last; VIQ: 44 first, 80 last). Despite his increase in IQ, Adam showed a persistently severe trajectory, with scores varying between 8 and 10 over seven assessments.

Case 2. "Bianca," a Caucasian female, was first seen at age 48 months as a clinical referral, at which point she received a diagnosis of autism. She was evaluated with ADOS Module 2 until age 5, when she received Module 3. Her mental ages were 46

months nonverbal and 56 months verbal at first assessment, and 107 months nonverbal and 120 months verbal at her 8.5-year-old assessment (NVIQ: 80 at first, 107 last; VIQ: 108 first, 126 last). Bianca showed decreasing autism severity over time, with scores dropping from 9 to 4 across six assessments.

Case 3. "Cara," an African American female, was first seen as part of a research project at age 3. She received a diagnosis of autism. She was evaluated consistently using ADOS Module 1. Her mental ages were 16 months nonverbal and 8 months verbal at first assessment, and 51 months nonverbal and 11 months verbal at her last assessment at age 10 (NVIQ: 47 at first, 40 last; VIQ: 23 first, 20 last). Despite the stability of her IQ scores over time, Cara showed worsening autism severity, with scores increasing from 5 to 10 over four assessments.

Case 4. "Daniel," a Caucasian male, was first seen at 34 months of age as a clinical referral and was given a nonspectrum diagnosis; at 46 months of age he received a PDD-NOS diagnosis which then remained stable over time. He was evaluated with ADOS Module 1 in his assessments through age 5; at age 10 he received Module 3. His mental ages were 38 months nonverbal and 36 months verbal at first assessment, and 162 months nonverbal and 142 months verbal at final assessment at age 10 (NVIQ: 112 at first, 129 at last; VIQ: 105 first, 113 last). Daniel showed consistently mild severity scores varying between 1 and 3 over four assessments.

Discussion

The calibrated severity metric based on ADOS raw totals offers a method of quantifying ASD severity with relative independence from individual characteristics such

as age and verbal IQ. It should have utility in various genetic, neurobiological, and clinical research endeavors, including treatment trials, that otherwise would use unstandardized ADOS raw totals. Calibrated scores have more uniform distributions across age- and language-groups compared to raw totals, making it possible to compare children's scores longitudinally across distinct algorithms. In part because of the modular system of the ADOS, chronological age, nonverbal IQ, and verbal and nonverbal mental age did not predict either raw totals or severity scores in this sample. The severity metric builds on this modular system to reduce the influence of participants' verbal IQ, which accounted for 10% of the variance in severity scores versus 43% of the variance in raw totals, a reduction from a large to medium effect size. The remaining influence of verbal IQ on the severity metric can be seen in the drift of mean scores toward greater severity in older age groups with lower language levels (Modules 1 and 2). This apparent age effect seems likely to be explained by lower verbal IQ in the older children without fluent speech. Though this effect has not been eliminated entirely, the calibrated metric is better able to measure autism severity beyond verbal impairment than are raw ADOS totals.

Calibrating scores within narrowly-defined age/language cells achieved the reduction in verbal IQ effects within the new metric and corrected for artificial variability in individuals' scores across time. Unfortunately, a greater number of calibration cells precludes a user-friendly age/language 'prefix' to the severity score, as mentioned in the introduction. The method described here necessarily defines autism severity in relation to individuals of similar age and language ability. When using these scores clinically and for research, one must keep in mind the age/language level of the child/sample, as there clearly will be developmental and adaptive functioning differences among children with

the same severity score on this 10-point scale. This is true of all standardized scores. Calibrated severity scores do not measure functional impairment, but are intended to provide a marker of severity of autism symptoms relative to age and language level. The module a child can be given depends on his/her expressive language level, and thus will continue to be an important indicator of adaptive functioning for most children.

The dataset described here included children from various areas in the United States, both urban and rural. Participants represented both consecutive clinic referrals and research participants. While this is likely a representative sample for a North American clinical research center, it is worth examining how referral bias might have influenced these calibrated scores. Though the dataset was large (N=1807 assessments from children with ASD), its division into age/language cells for calibration resulted in a few small cell sizes. For example, children under age 5 who are not language delayed are unlikely to be referred for an evaluation unless they exhibit notable ASD symptomatology, so we would expect these cells to have a more limited distribution in the higher end of the range of ADOS scores. Another referral bias involved the tendency for children of higher severity to have more clinic reevaluations than those with less pronounced features of ASD. Indeed, the mean severity scores across the 18 calibration groups ranged from 6.64 (in young children with fluent speech) to 8.10 (in older children with phrase speech only), indicating that severity scores are still somewhat influenced by developmental level and referral bias.

After attempting a number of methods for standardizing ADOS scores, we believe that the present method of using ADOS diagnostic classifications to ‘anchor’ severity scores best controls for recruitment effects that would be present in any large clinical

research sample, and therefore results in a metric more likely to be generalizable across datasets. If a cell in this calibration sample had predominantly high- or low-scoring children, this restricted range would only be assigned to severity scores associated with one classification (autism, ASD, or nonspectrum), allowing for more variability in other datasets across the other possible classifications. Ideally this method circumvents to some degree the inevitable effects of recruitment. Anchoring severity scores to ADOS classification instead of clinical diagnosis also avoids conflicting dimensional and diagnostic assignment. Within the present method, severity scores reflect ADOS raw totals regardless of the participant's diagnosis, so a child with a non-ASD best estimate diagnosis potentially could receive a score of 6 on the metric while a child with autism receives a 3, if the former child showed more autistic symptomatology relative to his/her age and language within that 45 minute assessment than did the child with autism.

More work is needed to test the validity and utility of this calibrated severity metric. Module change, especially into Module 3 (fluent speech), may inflate an individual's severity score. Some longitudinal variation in these scores is expected, but the purpose of the metric is to measure change beyond typical variation in ASD. For this reason, the fact that approximately 20% of ASD assessments with 'autism' ADOS classifications receive the highest severity score of 10, creating a ceiling effect, was preferred over drawing out the distribution of the metric with the result of less meaningful differences between scores. We hope to further examine patterns of severity score change over time in a longitudinal sample, identifying trajectory classes and the risk variables that predict class membership.

Another future direction is to calibrate the Social Affect and Restricted, Repetitive Behavior (RRB) domains of the revised ADOS algorithms separately in order to measure severity within these symptom domains. This process will need to employ a different method of mapping raw scores onto a severity metric, due to the fact that each domain has a smaller range of possible raw totals than the overall score (with a maximum of only 8 points for the RRB domain).

Limitations

Although based on a large sample, this is not a metric of symptom severity in a "true" ASD population because ADOS data on such samples do not exist at present. As larger population studies become available, the metric should be recalibrated within those samples for a more accurate reflection of the distribution of ADOS scores in the ASD population.

These results also may be influenced by the historical period in which some of the data were collected. This sample grew over a 16-year period in which patterns in ASD identification evolved. As greater numbers of children are identified at earlier ages (thus including milder cases at younger ages), it is possible that severity scores might have been assigned differently to raw totals if only recently collected data were used.

Conclusion

The ADOS calibrated severity metric represents a step towards achieving greater comparability of scores across time, age, and module, and is less influenced by verbal IQ than raw scores. Therefore, it should provide a better measure of ASD severity than other methods currently available, including ADOS raw total scores. This metric must be replicated in a large independent sample. To test the validity of the metric, calibrated

scores should be used to track observed changes in ASD severity against sources of convergent validity.

Calibrated scores could be used to predict outcome, changes in adaptive skills over time, and associations between severity of core features and clinical characteristics such as behavior problems, peer relationships, and school achievement. This metric may also prove useful in interpreting results from studies of the effectiveness of interventions, and in characterizing samples for genetic and neurobiological research. An important reminder, however, is that the calibrated severity metric is based on a relatively brief, office-based observation with a clinician, and thus is only one part of a necessarily broader picture of the strengths and difficulties of a child with ASD.

Table 2.1 Sample Description

DX		Module 1, No Words				Module 1, Some Words				Module 2, Younger than 5				Module 2, 5 or Older				Module 3			
		N	Mean	SD	Range	N	Mean	SD	Range	N	Mean	SD	Range	N	Mean	SD	Range	N	Mean	SD	Range
Autism	age	475	52.59	27.49	24-174	281	56.63	24.99	25-162	89	48.55	7.34	27-59	164	98.46	32.03	60-196	178	103.23	29.35	48-185
	viq	448	25.38	14.03	2-92	254	46.66	19.69	10-137	81	77.00	20.73	28-132	155	52.64	19.33	20-107	156	87.56	23.22	31-155
	nviq	442	52.34	21.20	2-144	253	65.82	20.54	14-122	77	90.44	22.87	52-170	155	77.25	23.98	24-131	158	92.98	23.57	34-155
	vma	453	11.39	19.05	1-291	251	25.29	30.59	0-353	82	42.94	50.09	21-357	157	54.91	53.34	13-354	151	87.50	44.66	3-369
	nvma	443	24.33	10.31	5-96	254	35.10	15.04	13-110	78	46.94	18.45	17-152	146	71.84	29.42	28-194	149	93.70	31.55	25-167
	ADI social	419	21.28	5.30	2-30	212	19.21	6.43	0-30	68	16.12	4.83	3-27	107	22.32	5.90	0-30	116	19.55	5.21	6-30
	ADI comm-V	5	17.40	4.09	12-22	74	15.05	4.50	0-24	64	15.41	3.99	3-22	101	18.18	4.11	0-26	116	16.99	4.30	7-25
	ADI comm-NV	419	11.74	2.34	0-14	212	9.89	3.35	0-14	68	8.57	2.93	0-14	107	10.36	3.25	0-14	116	9.27	3.27	2-14
	ADI-RR	419	4.79	1.72	0-10	212	5.41	2.20	0-10	68	6.34	2.59	1-12	107	7.04	2.07	0-12	116	7.50	2.72	2-12
	ADOS SA	475	17.29	2.34	5-20	281	14.87	3.38	1-20	89	12.93	3.45	2-20	164	14.47	3.39	6-20	178	11.39	3.87	0-20
	ADOS RR	475	4.92	2.02	0-8	281	4.43	2.00	0-8	89	4.51	1.98	0-8	164	5.12	1.95	0-8	178	3.44	1.94	0-8
PDD-NOS	age	76	38.03	13.48	24-107	114	43.84	17.78	24-175	108	42.77	9.98	24-59	51	78.96	18.33	60-129	250	101.98	31.26	42-195
	viq	74	35.68	15.67	7-75	107	66.78	20.02	11-129	83	84.50	20.57	2-149	44	63.93	17.56	28-102	230	100.93	21.19	49-164
	nviq	73	58.09	22.04	15-99	105	79.19	21.49	24-133	84	94.44	22.72	2-159	46	74.39	21.55	31-118	225	98.48	21.16	14-153
	vma	75	12.96	6.69	2-47	104	33.80	46.33	11-357	81	64.04	88.86	18-354	45	57.93	61.65	26-371	226	110.88	73.26	39-498
	nvma	73	20.34	6.72	7-34	105	40.10	47.87	16-507	80	41.66	13.30	23-91	44	59.07	13.05	34-90	208	102.30	36.22	37-190
	ADI social	72	15.15	5.67	3-25	94	11.57	6.49	1-28	65	10.72	5.11	2-25	33	14.82	7.23	4-29	174	14.93	7.43	0-29
	ADI comm-V	0	...	...	...	58	10.41	4.97	2-25	53	11.19	4.64	0-21	32	12.44	4.04	3-19	174	12.75	5.40	0-24
	ADI comm-NV	72	9.94	2.95	2-14	94	6.26	3.97	0-14	64	5.88	3.58	0-14	33	6.03	3.44	0-12	174	6.59	3.80	0-14
	ADI-RR	72	3.56	2.23	0-9	94	3.94	2.38	0-10	65	4.45	2.62	0-10	33	4.73	3.01	1-12	174	5.39	3.06	0-12
	ADOS SA	76	13.69	4.24	1-20	114	9.17	4.11	0-19	108	8.37	3.81	0-18	51	9.11	4.36	0-19	250	7.73	4.06	0-19
	ADOS RR	76	3.10	1.94	0-8	114	3.17	1.96	0-8	108	3.39	2.07	0-8	51	3.27	1.90	0-8	250	2.19	1.62	0-7
Non-spectrum	age	60	39.55	19.33	24-129	107	42.10	19.23	24-129	57	43.98	7.38	27-59	44	95.95	30.64	61-184	141	107.35	29.59	50-192
	viq	57	40.96	18.72	14-83	90	68.07	23.74	11-117	51	85.33	21.83	2-140	44	58.09	19.06	17-103	135	91.69	22.28	26-163
	nviq	55	58.80	28.72	13-132	89	70.52	23.74	15-116	49	92.04	20.46	2-133	44	61.93	24.13	24-118	136	89.85	22.23	35-151
	vma	57	13.77	5.63	1-26	87	27.62	8.34	13-52	50	56.62	75.44	17-356	43	50.14	13.94	20-77	134	103.18	61.51	32-492
	nvma	55	20.62	8.67	4-47	86	29.29	8.55	15-52	46	41.67	9.90	19-73	44	56.59	16.65	26-93	132	95.02	32.57	34-189
	ADI social	51	11.33	7.09	0-26	78	7.63	5.60	0-24	45	9.67	5.12	1-21	36	13.19	6.58	4-28	130	9.24	6.81	0-24
	ADI comm-V	0	...	...	...	38	5.53	3.32	0-13	43	9.70	5.04	1-21	34	11.00	5.09	2-23	130	8.27	5.46	0-24
	ADI comm-NV	51	7.73	4.22	0-14	78	4.29	3.26	0-12	45	5.22	3.68	0-14	36	6.17	4.08	0-14	130	4.32	3.72	0-14
	ADI-RR	51	2.59	1.94	0-8	78	2.32	1.73	0-8	45	4.04	3.31	0-11	36	4.25	2.54	0-10	130	3.65	2.69	0-11
	ADOS SA	60	8.36	5.82	0-20	107	4.71	3.91	0-17	57	3.56	2.77	0-15	44	4.16	3.14	0-10	141	3.90	2.94	0-14
	ADOS RR	60	1.88	1.87	0-7	107	1.40	1.49	0-7	57	1.49	1.42	0-5	44	1.63	1.64	0-5	141	0.98	1.15	0-5

Note. All ages in months. viq=Verbal IQ; nviq=Nonverbal IQ; vma=Verbal Mental Age; nvma=Nonverbal Mental Age; ADI social=ADI-R Social Total; ADI-R comm-V=ADI-R Communication Total for Verbal Subjects; ADI-R comm-NV=ADI-R Communication Total for Nonverbal Subjects; ADI-RR=ADI-R Restricted, Repetitive Behaviors Total; ADOS SA=revised algorithm Social Affect domain, ADOS RR=revised algorithm Restricted, Repetitive Behavior domain

Table 2.2 Mapping of ADOS Raw Totals onto Calibrated Severity Scores

ADOS Classification	Calibrated Severity Score	Raw ADOS Totals																							
		Module 1, No Words					Module 1, Single Words						Module 2, Phrases									Module 3, Fluent			
		2 yrs	3 yrs	4-5 yrs	6-14 yrs		2 yrs	3 yrs	4 yrs	5-6 yrs	7-14 yrs		2 yrs	3 yrs	4 yrs	5-6 yrs	7-8 yrs	9-16 yrs		2-5 yrs	6-9 yrs	10-16 yrs	
NS	1	0-6	0-6	0-3	0-3		0-3	0-4	0-2	0-2	0-2		0-2	0-3	0-3	0-3	0-2	0-2		0-3	0-2	0-3	
	2	7-8	7-8	4-6	4-6		4-5	5-6	3-4	3-4	3-5		3-5	4-5	4-5	4-5	3-5	3-5		4	3-4	4	
	3	9-10	9-10	7-10	7-10		6-7	7	5-7	5-7	6-7		6	6	6	6-7	6-7	6-7		5-6	5-6	5-6	
ASD	4	11-13	11-14	11-12	11-13		8-10	8-9	8-9	8-10	8-9		7-8	7-8	7	8	8	8		7	7	7	
	5	14-15	15	13-15	14-15		11	10-11	10-11	11	10-11		9	9	8-9	-	-	-		8	8	8	
	6	16-19	16-20	16-19	16-19		12-13	12-14	12-15	12-16	12-18		10-11	10-12	10-13	9-14	9-14	9-14		9-11	9-10	9-10	
AUT	7	20-21	21-22	20-21	20-22		14-16	15-17	16-18	17-19	19-20		12	13-14	14-16	15-16	15-17	15-17		12	11-12	11-12	
	8	22	23	22-23	23-24		17-19	18-19	19-20	20-21	21		13-14	15-16	17-18	17-20	18-21	18-20		13-15	13-14	13-14	
	9	23-24	24	24-25	25		20-21	20-21	21-22	22-23	22-23		15-17	17-18	19-20	21-22	22-23	21-23		16-17	15-17	15-17	
	10	25-28	25-28	26-28	26-28		22-28	22-28	23-28	24-28	24-28		18-28	19-28	21-28	23-28	24-28	24-28		18-28	18-28	18-28	

Note. NS= 'Nonspectrum' classification on the Autism Diagnostic Observation Schedule (ADOS); ASD= 'Autism Spectrum' classification on the ADOS; AUT= 'Autism' classification on the ADOS

Caption. To derive an ADOS calibrated severity score from a raw total, clinicians should first identify the relevant column from Table 2 based on the examinee's ADOS module / revised algorithm and chronological age within that module/algorithm group. The examinee's raw ADOS total is then located within the relevant column. The corresponding Calibrated Severity Score is the number in the second column from the left that falls within the same row as the examinee's raw total. It is worth noting that Calibrated Severity Scores are assigned even to those raw totals that do not meet classification thresholds of ASD or Autism on the ADOS, since clinical judgment can overrule the measure classification and result in a spectrum diagnosis.

Table 2.3 Raw Score and Calibrated Severity Score Means and Standard Deviations by Age/Language Cell (ASD Assessments Only)

		Algorithm Raw Total Score			Calibrated Severity Scores		
Group	**Age / Language Cell**	**N**	**M**	**SD**	**N**	**M**	**SD**
1	Mod 1, NW, Age 2	203	20.13	4.83	203	7.29	2.11
2	Mod 1, NW, Age 3	141	21.63	3.85	141	7.56	1.85
3	Mod 1, NW, Ages 4-5	130	21.96	3.63	130	7.87	1.48
4	Mod 1, NW, Ages 6-14	86	22.35	3.34	86	7.88	1.45
5	Mod 1, SW, Age 2	96	15.64	5.77	96	7.02	2.45
6	Mod 1, SW, Age 3	118	15.85	5.37	118	6.99	2.26
7	Mod 1, SW, Age 4	82	17.13	5.95	82	7.21	2.16
8	Mod 1, SW, Ages 5-6	68	18.84	4.71	68	7.48	1.72
9	Mod 1, SW, Ages 7-14	40	20.68	4.24	40	7.97	1.77
10	Mod 2, Phrases, Age 2	43	13.27	4.14	43	7.37	2.08
11	Mod 2, Phrases, Age 3	63	14.57	5.01	63	7.38	2.04
12	Mod 2, Phrases, Age 4	94	14.43	5.93	94	6.73	2.44
13	Mod 2, Phrases, Ages 5-6	103	16.84	5.78	103	7.45	1.99
14	Mod 2, Phrases, Ages 7-8	53	18.49	5.22	53	7.79	1.71
15	Mod 2, Phrases, Ages 9-16	59	19.16	4.48	59	8.10	1.37
16	Mod 3, Fluent, Ages 2-5	71	12.16	4.87	71	6.80	2.59
17	Mod 3, Fluent, Ages 6-9	236	11.66	5.19	236	6.64	2.55
18	Mod 3, Fluent, Ages 10-16	121	12.48	4.94	121	7.09	2.45

Note. Mod 1, NW=ADOS Module 1, No Words algorithm; Mod 1, SW=ADOS Module 1, Some Words Algorithm.

Table 2.4 Multiple Linear Regression Models for Calibrated Severity Scores and ADOS Raw Totals in ASD Assessments

	DV=Severity Score (ASD only, N=1465)					
	R^2	**F change**	**df**	**B**	**SE B**	**β**
Step 1[a]	.10	164.78	1,1463			
Constant*				8.5	.11	
Verbal IQ*				-.02	.001	-.32
	DV=Raw Total (ASD only, N=1465)					
	R^2	**F change**	**df**	**B**	**SE B**	**β**
Step 1	.43	1101.66	1,1463			
Constant*				24.14	.24	
Verbal IQ*				-.12	.004	-.66
Step 2[b]	.44	10.42	1,1462			
Constant*				24.05	.24	
Verbal IQ*				-.12	.004	-.67
Mat Ed*				.94	.29	.07

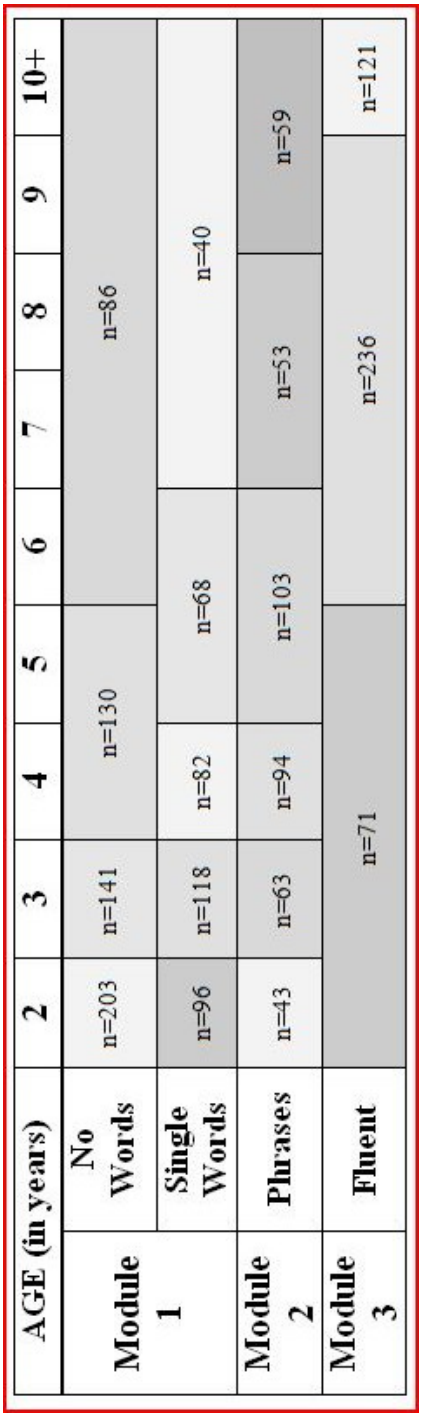
Note. DV=Dependent variable; Mat Ed=Dummy coded variable separating mothers with graduate or professional education to those of all other educational levels.

[a] All other variables excluded from the stepwise forward model.

[b] Change in R^2=.004 for Step 2 ($p<.001$)

* $p<.001$.

Figure 2.1. Age by Language Level Calibration Cells



Note. N's denote the number of ASD participants within each cell.

Figure 2.2. Distributions of ADOS Raw Total Scores by Age/Language Cells (ASD Assessments Only)

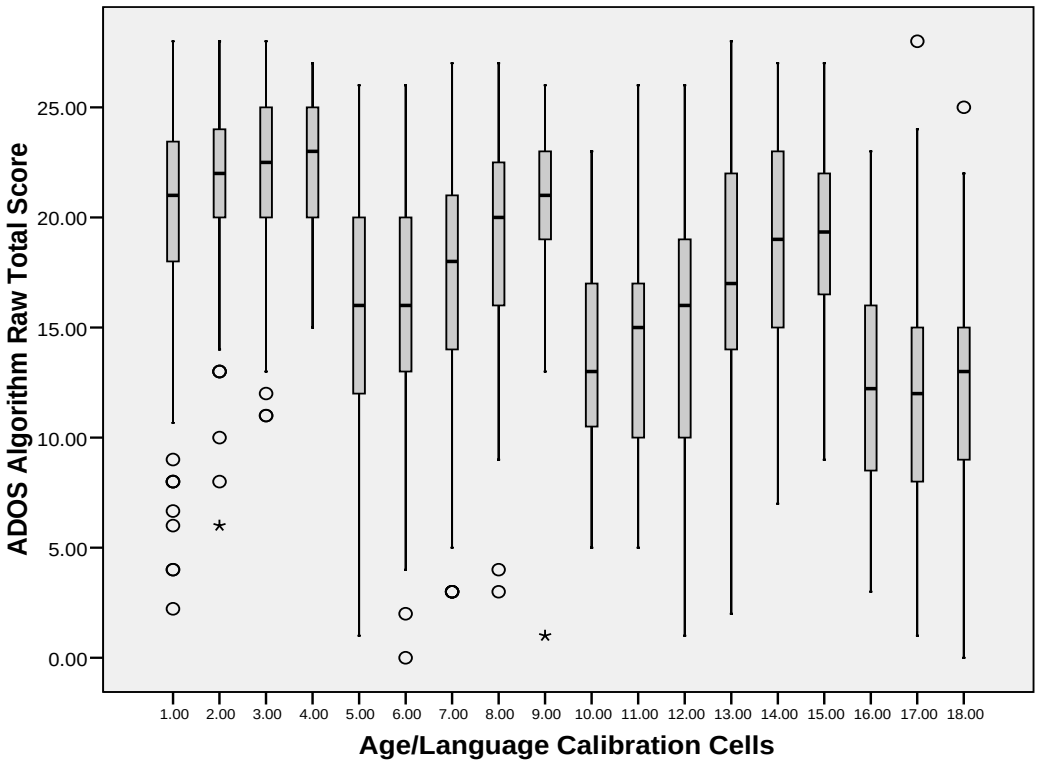


Figure 2.3. Distributions of Calibrated Severity Scores by Age/Language Cells (ASD Assessments Only)

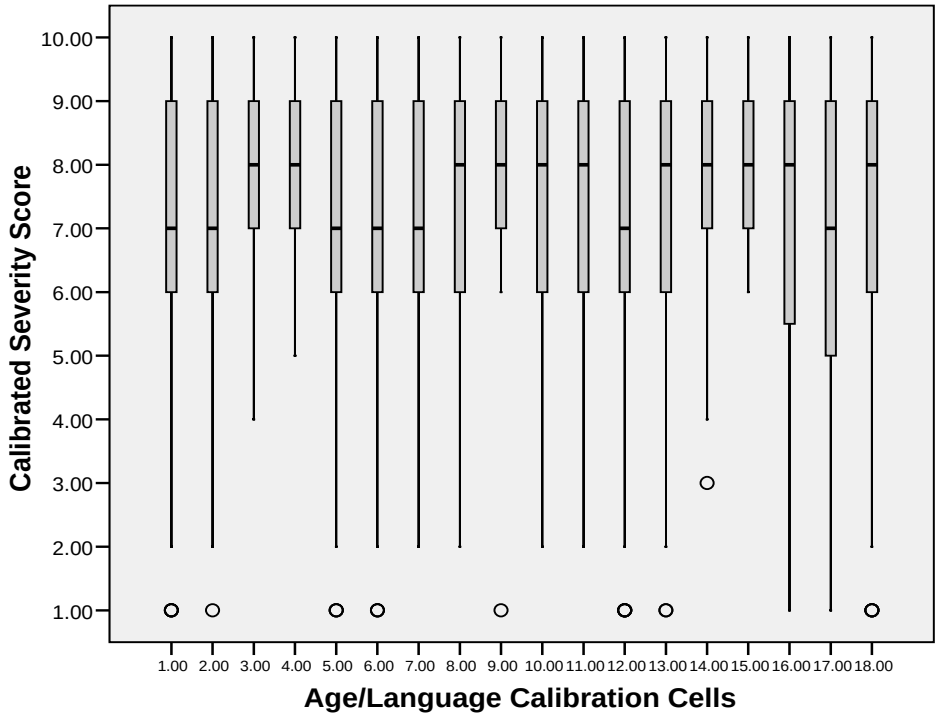


Figure 2.4. Distributions of Calibrated Severity Scores by Diagnostic Group

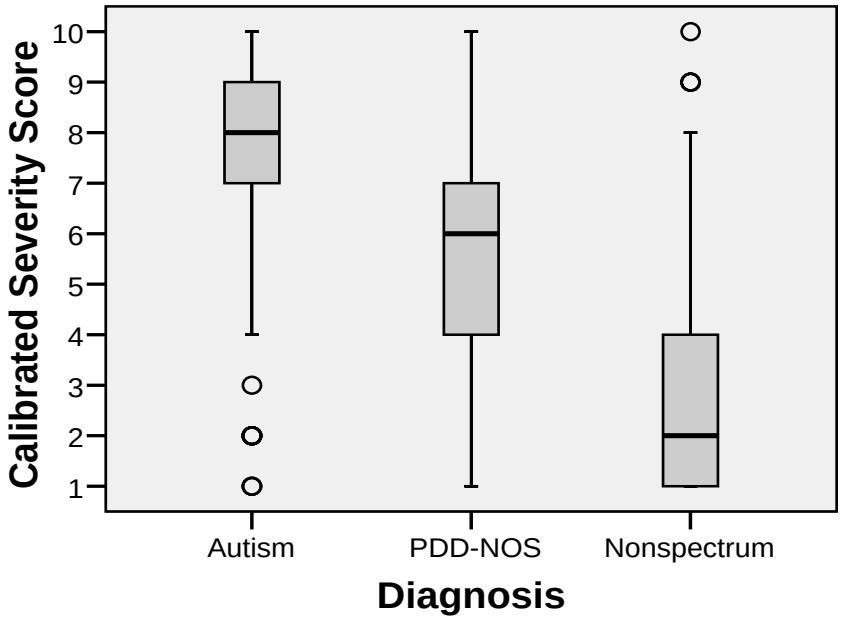
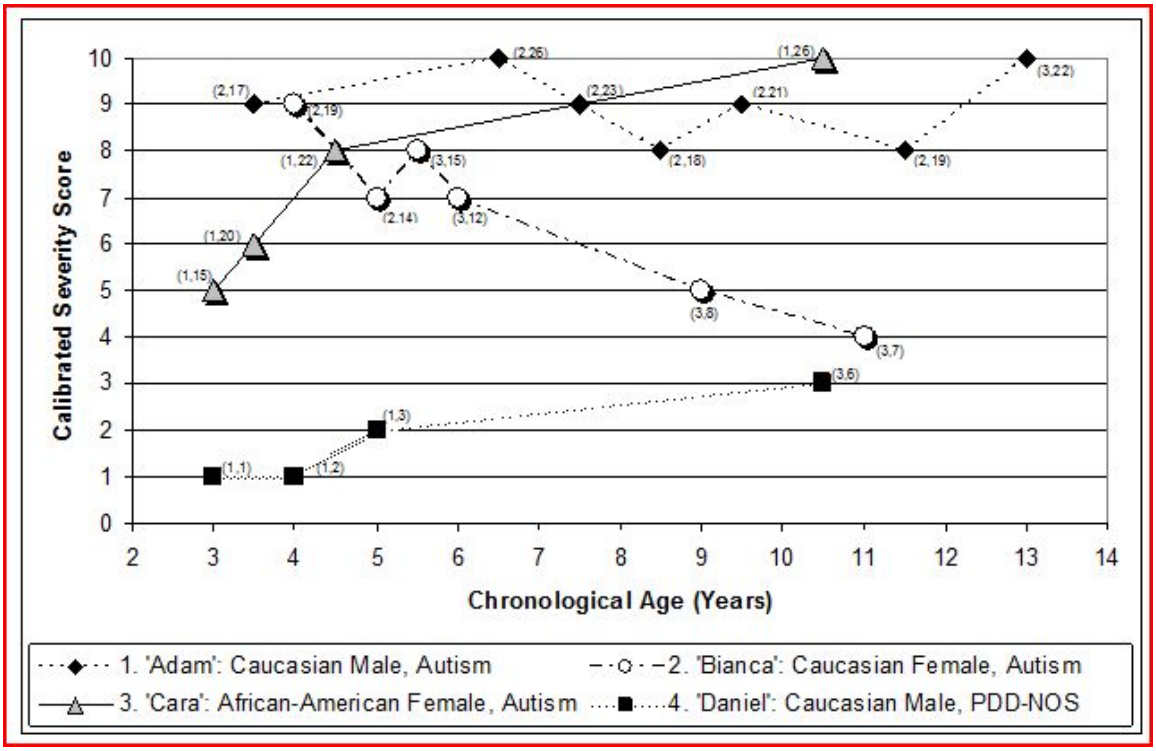


Figure 2.5. Case Summaries of Longitudinal Severity Scores



Note. Parentheses by individual data points indicate (*Module*, *Raw Score*) for each assessment.

Caption. The calibrated severity metric allows change across time and module to be evaluated in a standardized fashion in children of varying age and verbal ability. Adam and Daniel follow relatively consistent trajectories despite module changes, while a marked change in severity is apparent in Cara's scores despite seemingly small increases in raw total within the same module. Bianca's decreasing raw totals alone indicate a drop in ASD severity, but the clinical import of this is obscured by her module change and increasing chronological age. Severity scores are not necessarily more stable than raw totals, but were created to allow the change or consistency in these cases to be interpreted more readily than perceived patterns in raw total scores.

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Chapter III

Modeling Trajectories of ASD Severity in Children Using Standardized ADOS Scores

Over recent decades, the use of standardized assessment instruments (Lord et al., 2000; Rutter, Le Couteur, & Lord, 2003) has produced a strong research base for diagnosis of autism spectrum disorders (ASD). The same instruments have also contributed to proposed refinements to the current classification system, such as streamlining social and communication symptom domains to reflect a single underlying factor (Constantino et. al., 2004; Gotham, Risi, Pickles, & Lord, 2007; Robertson, Tanguay, L'Ecuyer, Sims, & Waltrip, 1999). With increasing amounts of carefully phenotyped longitudinal data available, these instruments may now be used to track changes in autism symptom profiles over time, potentially leading to more detailed prognostic estimates in ASD as well as opportunities to study the course of this disorder over the lifespan.

Research on ASD prognosis to date has largely focused on stability of diagnosis, verbal and cognitive outcomes, and symptom domain change over time. Using measures such as the Autism Diagnostic Interview – Revised (ADI-R: Rutter, Le Couteur, & Lord, 2003) or best-estimate diagnoses influenced by the ADI-R, the Autism Diagnostic Observation Schedule (ADOS: Lord et al., 2000) and clinical judgment, stability of ASD diagnosis has been most recently reported between 63% and 98% (Cederlund, Hagberg,

Billstedt, Gillberg, & Gillberg, 2008; Eaves & Ho, 2008; Lord et. al, 2006; McGovern & Sigman, 2005; Turner, Stone, Pozdol, & Coonrod, 2006; Turner & Stone, 2007). Lower estimates often reflect changes within the autism spectrum and/or in younger samples (McGovern & Sigman, 2005; Turner & Stone, 2007). However, diagnostic stability as high as 88% has been reported across larger time spans beginning in early childhood (Eaves & Ho, 1996; Turner, Stone, Pozdol, & Coonrod, 2006).

Studies of cognitive outcome have had more variable conclusions. Distinct IQ trajectories have been noted in the ASD population; groups with initially higher IQs often make great gains while lower functioning groups remain relatively stable or show small improvements over time (Anderson et. al., 2007; Gabriels, Hill, Pierce, Rogers, & Wehner, 2001). By contrast, the small sample of children with ASD (N=26) described by Turner and co-authors (2006) showed remarkable cognitive gains between ages 2 and 9, with just 16% of the sample above the range of intellectual disability (e.g., IQ>=70) at first assessment compared to 72% at final follow-up. Sigman and McGovern (2005) also reported cognitive and language gains between preschool and mid-childhood for a third of their sample, followed by stability or slight decline from mid-childhood through adolescence/adulthood. Charman and colleagues (2005) added the caveat that stable group means in cognitive scores within their sample masked considerable individual variability across early to mid-childhood, a finding replicated in a longitudinal sample of children with ASD measured in mid-childhood and again as adults (Farley et. al., 2009). Comparing longitudinal change in cognitive ability across these and other studies is complicated by the different reliability properties of specific IQ tests used.

Within the small but growing body of literature on trajectory of ASD-specific symptom expression over time, severity has most often been quantified with scores from the ADI-R and the Childhood Autism Rating Scale (Schopler, Reichler, & Renner, 1986). The 2004 Seltzer, Shattuck, & Abbeduto (2004) review indicates collected findings of general improvement over the lifespan in the three core DSM-IV (American Psychiatric Association, 1994) symptom domains, including improvement in reciprocal social interaction and communication and a diminishing of restricted and repetitive behaviors. Yet clear impairment remained in adulthood across all three domains. Communication skills often improved most, with the greatest stability of symptom expression observed in restricted, repetitive behaviors.

In the Seltzer review as well as in more recent empirical studies, improvement was noted in *social reciprocity* across various ages: from ages 12-19 (McGovern & Sigman, 2005); between adolescence/adulthood and retrospective reports of age 5 (Piven, Harper, Palmer, & Arndt, 1996); and between reports of age 4-5 and current reports at age 7 (Charman et. al., 2005). Continued impairment was always associated with these gains, however, (Billstedt, Gillberg, & Gillberg, 2007) and one study reported a slight worsening in social skills in children with autism assessed between ages 4-6 and again two years later (Howlin, Mawhood, & Rutter, 2000). Because *communication skills* are defined and measured in various ways (e.g., as verbal IQ, verbal proficiency level, social/pragmatic use of language, or nonverbal communication), the magnitude of improvements can be difficult to compare across studies. Improvements in absolute levels of verbal or communication skills for samples with autism have been reported (Anderson et. al., 2007; Charman et. al., 2005; Howlin, Mawhood, & Rutter, 2000; Mawhood,

Howlin, & Rutter, 2000; Sigman & McGovern, 2005; Starr, Szatmari, Bryson, & Zwaigenbaum, 2003) with little evidence of decline. *Restricted, repetitive behaviors* had the most variable outcome across time, with reports of improvement (decreased totals on this ADI-R domain across ages 12-19; McGovern & Sigman, 2005), variability in outcome across age groups and samples (Billstedt, Gillberg, & Gillberg, 2007; Charman et. al., 2005), and stability across time in this symptom domain (Piven, Harper, Palmer, & Arndt, 1996; Starr, Szatmari, Bryson, & Zwaigenbaum, 2003). While the research attention paid to autism trajectories is encouraging, it is challenging to build a coherent picture of stability and change in ASD over time given the variability of participant demographics (e.g., chronological age, developmental level), measures used, and study design (e.g., retrospective versus prospective data analysis). Sample and method differences within the literature may mask patterns in symptom gains or losses in subgroups on the spectrum, if such do indeed exist.

Another obstacle in plotting the trajectories of ASD symptom expression is that the ADOS is often a primary measure used in phenotyping research samples. Although the modular format of this measure contributes to its strong predictive validity across age and developmental levels, this aspect of the ADOS makes longitudinal comparisons difficult. In each of four developmental- and language-level dependent modules within this standardized assessment instrument, a protocol of semi-structured social activities is administered and scored by a trained examiner. Specific items comprise an algorithm for each module, which yields a classification of "autism," "autism spectrum disorder," or "nonspectrum." The ADOS has shown strong diagnostic sensitivity and specificity against best estimate diagnoses (Gotham, Risi, Pickles, & Lord, 2007), making it a

common choice among phenotyping measures. Comparing ADOS data over time, however, is confounded by observed effects of age and language level on algorithm or domain total scores (Gotham, Risi, Pickles, & Lord, 2007; de Bildt et. al., 2004; Joseph, Tager-Flusberg, & Lord, 2002). Additionally, as a child ages or gains language skills, he or she often moves through ADOS modules, making raw scores even less directly comparable across time.

Two recent updates have been made to the ADOS with the purpose of increasing the comparability of the modules used with children and adolescents. First, revised algorithms were created with the same number of items and of similar content across modules 1-3 (Gotham, Risi, Pickles, & Lord, 2007). Five new algorithms correspond to specific developmental groups within these three modules, resulting in minimal association between ADOS totals and chronological age, generally decreased association between ADOS total and verbal IQ when compared to the original algorithms, and improved predictive validity of the measure in most developmental groups (Gotham et. al., 2008; Gotham, Risi, Pickles, & Lord, 2007). Second, ADOS revised algorithm raw total scores were standardized within 1807 cases from participants with ASD to produce a calibrated severity metric (Gotham, Pickles, & Lord, 2009; see Chapter 2). This 10-point scale was proposed as an alternative method of quantifying ASD severity on the ADOS with greater independence from participant characteristics such as chronological age and IQ. The resulting metric showed more uniform distribution across age- and language-level determined groups than did raw total scores. Standardization also reduced the percentage of variance accounted for by verbal IQ from 43% using raw totals to 10% using severity scores. It is important to note that calibrated severity scores do not measure

functional impairment but rather provide a marker of ASD severity on the ADOS benchmarked to be consistent with diagnostic category and relative to age and language level. Used for this purpose, the metric provides a solution for comparing ADOS scores across modules and time. Because the standardization was not based on a population sample, however, the scores may be subject to recruitment effects.

The present study uses standardized ADOS scores to plot changes in ASD severity over time in a mixed prospective cohort. The primary goal is to identify latent trajectory classes, or patterns of change over time, in autism severity in children and adolescents. Because cognitive functioning has been found to influence ASD symptom presentation (Bishop, Richler, & Lord, 2006; Gabriels, Hill, Pierce, Rogers, & Wehner, 2001; Joseph, Tager-Flusberg, & Lord, 2002; Matson, 2007), the design included covarying both verbal and nonverbal IQ (as well as other participant characteristics such as gender and race) in the modeling of ASD severity trajectory classes. A further aim is to compare trajectories of IQ and measures of adaptive functioning for each of the resulting ASD severity trajectory classes.

Methods

Participants

Analyses were conducted on data from 345 individuals referred for ASD evaluations. Inclusion criteria required repeated ADOS administrations with contemporaneous best estimate clinical diagnoses, verbal and nonverbal IQ scores, and complete data on gender and racial affiliation. The final dataset included 1026 cases, where 'case' is defined as contemporaneous ADOS data and a best estimate clinical

diagnosis. Final (i.e., most recent) diagnoses of autism were assigned to 231 individuals (67% of all cases); 104 individuals received final diagnoses of Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS; 30% of all cases); and 10 individuals (3% of all cases) ultimately received nonspectrum diagnoses, though they were clinically referred for ASD and were given an ASD diagnosis at one or more assessments. Five of these participants had final diagnoses of language disorders, two had intellectual disability, one each had Tourette's disorder, a mood disorder, or Oppositional Defiant Disorder with ADHD. Data from participants identified as 'nonspectrum' at all longitudinal time points were not included in this sample in order to model severity trajectories within the autism spectrum.

Chronological ages in the sample ranged from 2 to 15 years. Female participants (n=63) contributed data for 18% of all cases. Ethnicities represented include 18% African American cases (from 62 individuals); 2% Asian American (n=7 individuals); 78% Caucasian (n=272); 1% biracial (n=3); and one participant who selected 'other.' Twenty-five percent of the sample reported maternal education at the graduate or professional level; 21% of mothers had a high school degree or less.

Within this sample, 159 individuals were consecutive referrals to the Treatment and Education of Autistic and Communication Handicapped Children (TEACCH) Centers at the University of North Carolina, Chapel Hill, and the University of Chicago Developmental Disorders Clinic who participated in a longitudinal study of the "Early Diagnosis of Autism Spectrum Disorders" conducted through these universities. These participants were referred for possible autism before 36 months of age, and most were evaluated again around ages 5 and 9. For more detailed information on the data collection

procedures associated with this study, see the methods reported in Lord (1995), and Lord et al., (2006). The remainder of participants (186 individuals) in the current sample received diagnostic evaluations as clinic patients or participants of various research projects at the University of Michigan Autism and Communication Disorders Center (UMACC) or University of Chicago clinic, and then returned for self- or school-referred clinical reevaluations or received another evaluation through a research project at these clinics. Out of 345 total participants with repeated assessments through clinic reevaluations or longitudinal research, 258 individuals had 2 or 3 ADOS assessments, and 87 had between 4 and 8 assessments.

Measures and Procedure

A standard research protocol was employed across sites and projects. This included the initial administration of the Autism Diagnostic Interview – Revised (Rutter, Le Couteur, & Lord, 2003), a standardized, semi-structured interview of parents and caregivers for the purpose of taking a developmental history specific to ASD features, followed by the Vineland Adaptive Behavior Scales (VABS), 1st or 2nd edition (Sparrow, Balla, & Cicchetti, 1984; Sparrow, Cicchetti, & Balla, 2005), a standardized parent/caregiver interview of adaptive functioning across social, communication, daily living, and motor skills domains. Next, a child assessment took place, which included psychometric testing and the ADOS. An alternative protocol was a re-evaluation consisting of the child assessment only. In both cases, a clinical diagnosis was made by a psychologist and/or psychiatrist after review of all data. The ADI-R was available for 328 individuals and the Vineland for 330 individuals. The ADOS was administered and scored by a clinical psychologist or trainee who met standard requirements for research

reliability. The Pre-Linguistic Autism Diagnostic Observation Schedule (PL-ADOS: DiLavore, Lord, & Rutter, 1995) was given in 350 cases (34%) and the toddler module of the ADOS (Luyster et. al., 2009) was given in 37 cases (4%); for both measures, identical items were recoded to Module 1 algorithm scores. A developmental hierarchy of cognitive measures, most frequently the Mullen Scales of Early Learning (MSEL: Mullen, 1995) and the Differential Ability Scales (Elliot, 1990), determined IQ scores.

Research-only participants received financial compensation and a written summary of evaluation results. Clinic-referred participants received oral feedback and a written report without financial compensation. Institutional Review Boards at the University of North Carolina, Chicago, or Michigan approved all procedures.

Research Design and Statistical Analyses

ADOS calibrated severity scores (Gotham, Pickles, & Lord, 2009) for participants with longitudinal data were analyzed for patterns of stability or change using the Generalized Linear Latent and Mixed Models, or gllamm, procedure (Rabe-Hesketh, Skrondal, & Pickles, 2004) in Stata version 10 (StataCorp, 2007). Mixed-effects models resulting in 3 to 6 trajectory classes with linear and quadratic random dimensions were compared for goodness of fit (Pickles & Croudace, in press). Models were fitted first without and then including the baseline covariates verbal IQ, nonverbal IQ, gender, and race, and the most parsimonious model was chosen. The linear fixed part coefficients, representing linear and quadratic relationships of age with ADOS severity scores for the whole sample, were tested for significance using an overall likelihood ratio Chi-square test to determine whether there was evidence of a common trend for all individuals.

Baseline covariates were examined for significance as predictors of the model-assigned latent class membership using multinomial logistic regression.

In order to examine the concurrent development of the VABS Daily Living Skills V-scale scores and Verbal IQ, we plotted the smoothed (fractional polynomial) mean scores by age for each trajectory class. Wald-tests from GEE multivariate regression models with an exchangeable working correlation matrix (which are equivalent to repeated measures ANOVA but not requiring complete data and with the use of the robust parameter covariance matrix estimator not assuming a constant error variance) were used to test for class differences in the intercept (centered at age 6 to allow intercepts to provide estimates of class means at this point), linear, and quadratic trends. Finally, we used an overall likelihood ratio Chi-square test to examine trajectory class differences in treatment variables representing total number of hours of parent training with TEACCH techniques and total hours of parent training in Applied Behavior Analysis (ABA) techniques by age 5 (see Anderson, Oti, Lord, & Welch, 2009, for a more detailed description of these treatment variables); this analysis was run only on the subsample of data collected through the "Early Diagnosis of Autism Spectrum Disorders" longitudinal study.

Results

Latent classes by ADOS severity score trajectory

A linear model of five latent trajectory classes was found to have the most parsimonious fit to longitudinal ADOS severity score data in this sample, as suggested by the lowest Bayesian Information Criteria (BIC) in comparison to other models (see Table

3.1). A greater number of dimensions or classes led to models with higher BIC. The linear fixed part coefficients of the five class model showed no evidence of a significant relationship between ADOS severity and chronological age in the sample ($\chi^2(2)=0.33$, $p=0.8$), suggesting there was no significant overall age trend masked by the grouping into latent classes.

One of the five classes in this best fitting model included only 6 participants (one with autism, two with PDD-NOS, and three with nonspectrum final diagnoses [intellectual disability (n=1); language disorders (n=2)]). These children, who had a total of 22 assessments, appeared to have stable mild severity scores in the range of 1 to 3 over time, with one outlying assessment case receiving a severity score of 6. Because of the small size of this class, these participants were dropped from further analyses. The four remaining latent trajectory classes are shown in Figure 3.1. Participant chronological age was restricted to a maximum of 10 years for graphical representation of the data, because data for the 11-15 age span were sparse and thus less reliable. The four classes included a persistent high severity class (Class 1: Persistent High; 46% of observed data in the sample), a moderately severe class (Class 2: Persistent Moderate; 38%), a class that tended to increase in ASD severity over time (Class 3: Worsening; 9%), and a class that decreased in ASD severity over time (Class 4: Improving; 7%). The average probability with which children were assigned to their best class was high for classes 1, 3, and 4 (0.82, 0.79 and 0.81 respectively), but was rather lower (0.68) for class 2 (Persistent Moderate). The average probability that children assigned to this class might have belonged to class 3 (Worsening) was not small (0.21). As suggested by our labeling, 70% of the Worsening class exhibited worsening scores, but the remaining 30% showed

variability across time, some of them "ending" on an improving score. By contrast, all children assigned to the Improving group had most recent severity scores milder than previous scores. Table 3.2 describes initial and final diagnostic measures and demographic variables of the 339 participants assigned to the four latent classes. ADI-R domain totals are reported as sums of "Current" scores of only those algorithm items comparable across age groups at both initial and final assessment, in order to compare stability or change over time by latent class. Trends in raw scores were observed to fall (e.g., improve) slightly over time in Current Social-Communication scores on the ADI-R and Social Affect scores on the ADOS, and to rise (e.g., worsen) slightly over time in Restricted Repetitive Behavior scores across the first three classes. The Worsening class was the only group to exhibit greater severity over time in any ADI-R Current domain mean score (Verbal Communication and RRB). Not surprisingly, ADOS raw scores (which highly influence the calibrated severity scores on which the model was based) showed dramatic improvement in the Improving class alone.

Covariates as predictors of latent class membership

As shown in Table 3.2, gender, race, and nonverbal IQ did not significantly predict latent class membership in multinomial logistic regression analyses of the covariates at initial assessment. However, initial verbal IQ was a significant predictor: higher verbal IQ predicted membership in the Improving, Worsening, and Moderate classes over the Persistent High class. Relative risk ratios (RRR) were generated from multinomial logistic regression analyses of the covariates; for this procedure, race and gender were entered as binary predictors (0=Caucasian or Male; 1=Other Race or Female), and verbal and nonverbal IQ scores were standardized. RRRs indicate the

multiple of odds for specific class membership (e.g., Improving) in a particular group (e.g., females) as compared to membership in the Persistent High class, used here as the reference group. A one standard deviation difference in verbal IQ increased the odds of being in the Moderate class, relative to the Persistent High class, by 63%, and of being in the Improving class, relative to the Persistent High class, by 383%. Though not statistically significant, it was noteworthy that minority race status increased the odds of being in the Worsening class by 113%.

Diagnosis and regression status by latent severity class

The majority of participants in the Persistent High and Moderate classes had final diagnoses of autism (88% and 64% respectively), while most children in the two smaller classes had PDD-NOS diagnoses (60% of Worsening and 78% of Improving class members). Similarly, the majority of children with autism was assigned to the most prevalent and stable groups, 60% in Persistent High and 36% in Moderate. Participants with PDD-NOS most commonly were assigned to the Persistent Moderate class (45%), with 17.3% each in Worsening and Improving. Three children in the Worsening severity class ultimately received nonspectrum diagnoses, one child each with language disorder, disruptive behavior disorder, and intellectual disability. Four children in the Improving class received a nonspectrum final diagnosis (n=1 Tourette's syndrome, n=1 mood disorder, and n=2 language disorders).

Classes were assessed for differences in rates of parent-reported regression in communicative or other skills, as measured by scores of 1 or 2 on Items 11 or 20 of the ADI-R. Mean age of regression across the sample was 17.1 months for language losses (SD=4.6) and 21.3 months for non-language loss (SD=15.9), indicating that most

significant losses took place before the initial data collection point in this sample. Language regression scores did not differ significantly across the four classes, F (3, 439) = 2.3, p = .08. The Worsening class had the lowest percentage of language loss of any of the trajectory classes, and also did not show prevalent loss of other skills compared to the remaining classes. As expected, regression does not appear to be a primary contributor to the increasing severity trend noted in this class. Losses in language skills were most prevalent in the Improving class, which may suggest that these children were developing at faster rates even in infancy and toddlerhood, and thus tended to have developed language (and then exhibited losses) while members of other severity classes had not.

IQ and adaptive behavior trajectories by latent severity class

The pattern of mean Verbal IQ standard scores and VABS Daily Living V-scale standard scores over time in each of the four trajectory groups are shown in Figures 3.2 and 3.3. All classes showed an improving trend in Verbal IQ measurements but with marked differences (GEE Wald test of intercept, linear and quadratic terms $\chi^2(9)=219.60$, $p<.001$). The Improving class means exhibited a much steeper curve indicating progress that was both more rapid and greater than experienced by participants in the other three classes. Verbal IQ of these Improving class participants appeared to become stable between 6 and 7 years of age. Tests at age 6 indicated the Improving class was significantly higher than the Persistent Moderate ($p<.001$) and Worsening ($p<.001$) in mean scores; the latter two were similar ($p<.164$) though above the Persistent High class ($p<.001$ for both classes).

On the Vineland Daily Living Skills score (including such skills as toileting, bathing, dressing, chores, etc.), the classes show quite similar and relatively unimpaired

scores at age 2, but diverge thereafter (GEE Wald test over intercept, linear and quadratic $\chi^2(9)=103.16, p<.001$). Modest gains are made by the Improving class, with marked declines noted in the three other groups. By age 6 the Improving class is significantly better than the other three classes (at p=0.006 or smaller), with no significant differences among these three (p=0.243 or greater).

Trajectory class differences in parent training variables

Using data from the "Early Diagnosis of Autism Spectrum Disorders" longitudinal subsample described in this paper, Anderson and colleagues (2009) found that individuals who, as young children, participated in more than 20 hours per week of mentored, parent-implemented structured teaching (MPST; a home teaching program using TEACCH techniques) had substantially greater increase in adaptive social behavior age equivalents on the VABS Socialization domain at age 13 than did children with less or no exposure to MPST. No effects were found for hours of parent training in ABA by age 5 in the same sample. We ran Chi-squared analysis of both parent training variables (see Anderson et al., 2009, for detailed description) to assess for differences within the severity trajectory classes, and found no significant class difference in level of parent training for either intervention technique, $\chi^2(6)=7.1$, p=.32 for MPST and $\chi^2(6)=7.8$, p=.25 for ABA.

Discussion

Latent trajectory class analyses of ADOS standardized severity scores in a longitudinal sample indicate that a four class linear model best represents these data. The

latent severity trajectory classes include prevalent Persistent High and Persistent Moderate severity classes, and small Worsening and Improving severity classes.

A persistently mild severity class consisting of just 6 participants was also observed, though dropped from further analyses. The low prevalence of this class may be due to recruitment or referral biases, in that families of children who continued to have only mild expression of autism symptoms likely chose not to return to clinics or continue in research for repeated evaluations and recommendations. In general, however, the inception cohort of children initially diagnosed at age 2, which made up the majority of this sample, maintained a high level of participation over time, with 80.4% follow-up rate at age 9 (Lord et. al., 2006). According to a report on this cohort, attrition was higher in families with non-white ethnicity but was unrelated to initial diagnosis, language level, IQ, adaptive functioning, or gender (Lord et. al., 2006). If the low prevalence of the mild class was solely a recruitment issue, we would expect the mild class to be larger in this subsample which had low attrition rates unrelated to improving symptoms.

The association of the latent classes with the baseline covariates of verbal IQ, nonverbal IQ, gender, and race was examined. Verbal IQ was the only significant predictor of class membership, with higher scores predicting membership in Improving, Worsening, and Moderate classes over the Persistent High severity class. Because the youngest age of assessment in this sample, 24 months, is at the end of the average range of autistic regression (Luyster et. al., 2005), we did not expect that regressions occurring during the study period would greatly influence the trajectory of ASD severity in these analyses. Indeed, percentages of reported losses in verbal skill were lowest in the

Worsening class, indicating that the increase in ASD symptoms in this class was not the same as that which parents report as regression.

Diagnostic differences also map onto severity trajectory classes. The majority of participants in the Persistent High and Moderate classes had final diagnoses of autism, and similarly the majority of children with autism were members of these classes. The majority of children with PDD-NOS were assigned to the Persistent Moderate class. Most children in the Worsening and Improving classes had PDD-NOS diagnoses. Only three children in the Worsening severity class and four in the Improving class ultimately received nonspectrum diagnoses. While there will always be children with unclear clinical presentations, it is interesting to see how these difficult cases are represented in ASD severity trajectories. The Worsening class as a whole may be thought of as an unusual group, with a mixed presentation on both ADOS calibrated severity metric scores (with the majority worsening but others variable) and current ADI-R domains (i.e., improving Social and Nonverbal Communication mean scores and slightly worsening Verbal Communication and RRB scores). These trends warrant further exploration in other datasets.

Again, by using calibration cells to derive the standardized ADOS scores, 'autism severity' is defined only in relation to children of similar age and language ability, and is therefore not a measure of functional impairment. However, the differences in IQ and adaptive behavior noted across these trajectory classes (e.g., lowest IQ mean in the Persistent High severity class) indicate that severity of autism characteristics continues to be strongly linked to cognitive and adaptive functioning – at least in the forms of measurement we have available.

We did not find class differences in TEACCH-based or ABA parent training hours by age 5 in the longitudinal study subsample. Though Anderson and colleagues did note effects of the TEACCH-based training on VABS social domain age equivalents at age 13, they acknowledged that this was not a randomized controlled trial of this intervention. Data were based on parent report of treatment or training received, with no checks on quality or actual implementation of intervention. Further, children who are more severely impaired tend to be enrolled in more hours of intervention, which may obscure treatment effects in severity class analyses such as this one. Future examination of trajectory class differences in carefully controlled intervention data is needed.

Limitations

All longitudinal data available in the UMACC database were used in this sample, including an inception cohort assessed at ages 2, 3, 5, and 10, as well as clinic patients and research participants with multiple ADOS administrations over time. Though the inception cohort comprised the majority of the sample, we would expect caregivers of clinic patients to self-refer for repeated evaluations more often in the case of persistently severe autism characteristics. Therefore we would expect the high and moderate severity groups to be more prevalent due to recruitment or referral bias, as was observed. Similarly, because they were identified at early ages despite a historical context of limited public awareness of ASD, the group of children comprising the inception cohort is likely to have lower IQ and higher ADOS scores (e.g., a more severe sample; Richler, Bishop, Kleinke, & Lord, 2007) than samples diagnosed at age 2 in more recent years. Thus the present sample is likely skewed toward higher average severity than we would expect to see in a population cohort. For a related discussion of the representativeness of the

sample used in the ADOS severity score standardization, see Gotham et al., 2009. Other limitations include the possibility that changing to a more demanding language-based ADOS module may artificially inflate an individual's severity score, though evidence for this has not been apparent in our samples.

Conclusions

Insight into the direction, magnitude, and age periods associated with ASD severity changes would aid clinical prognostic estimates and the study of developmental trajectory of these disorders. However, more longitudinal and epidemiological research is needed to distinguish the appearance of ASD severity subgroups from the developmental differences of samples tested at different ages. Before these trajectory class findings can inform research and clinical practice, it is crucial that analyses be replicated in large datasets with less recruitment bias, such as the longitudinal Pathways Study in Canada that follows all children with ASD diagnoses in a given province (Szatmari et. al., 2010), or the epidemiological dataset associated with the Autism and Developmental Disabilities Monitoring (ADDM) Network (Centers for Disease Control, 2006). Future directions include exploration of the effects of other risk variables on class membership, as well as study of the association between trajectory classes and distal outcomes such as academic placement and peer relationships. Further evidence for multiple 'autisms' (DeLong, 1999; Morrow et. al., 2008; Pelphrey, Adolphs, & Morris, 2004) may lead to inclusion of severity trajectories as an aspect of ASD phenotyping.

Table 3.1. Latent Severity Class Model Comparison

Classes Dimensions	4	5	6
Intercept	2148.5 (4355.4)	2148.8 (4367.1)	
Intercept Linear slope	2134.2 (4344.4)	**2122.8** **(4339.1)**	2115.2 (4341.4)
Intercept Linear slope Quadratic slope	2133.6 (4360.6)	2120.9 (4358.7)	2110.7 (4361.7)

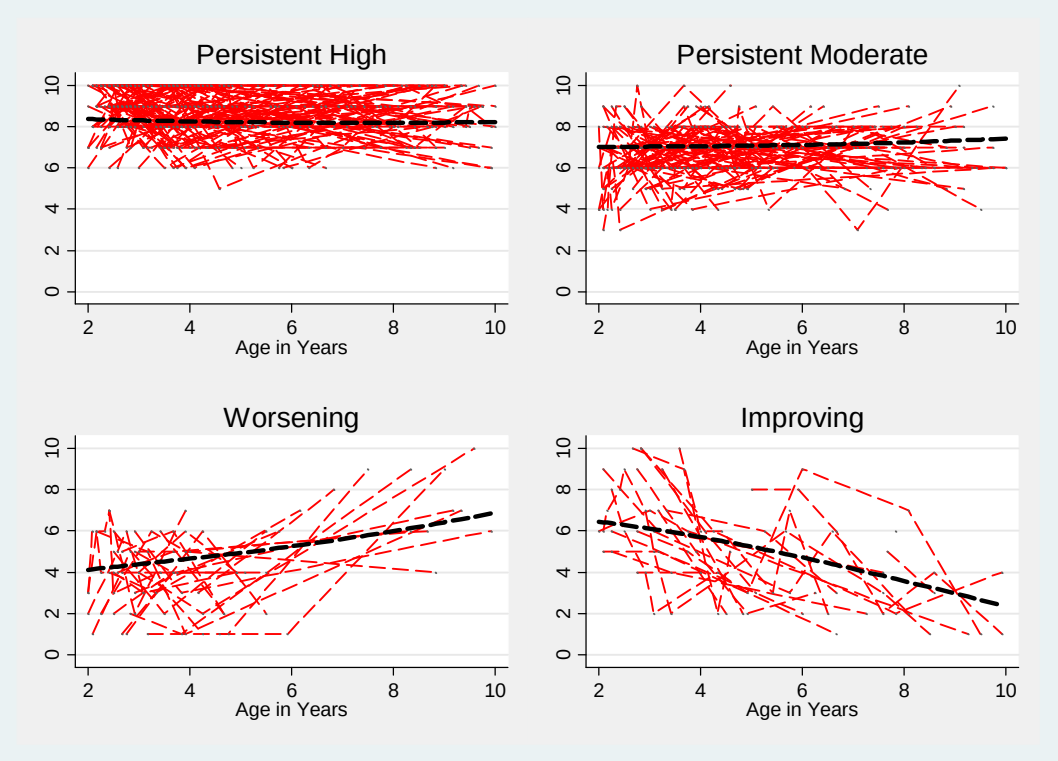
Note. Log-likelihoods shown, with Bayesian Information Criteria (BIC) below them in parentheses. Lowest BIC = most parsimonious fitting model (in bold type).

Table 3.2. Latent Severity Classes: Descriptives and Predictors

		Class 1		Class 2		Class 3		Class 4	
		Persistent High		Persistent Moderate		Worsening		Improving	
		First	Last	First	Last	First	Last	First	Last
Age (Years)	M(SD)	3.4(1.6)	7.5(2.7)	3.3(1.3)	7.0(2.7)	2.8(.6)	7.3(3.0)	3.4(1.7)	7.5(2.7)
ADI-R (C) Social	M(SD)	13.5(4.6)	12.3(5.0)	11.3(4.9)	10.2(5.2)	8.3(4.0)	5.6(3.6)	9.4(5.3)	6.7(5.4)
ADI-R (C) Comm Verbal	M(SD)	9.9(4.1)	9.8(4.4)	8.5(4.1)	8.3(4.1)	5.4(2.5)	5.8(3.2)	5.3(4.4)	5.3(4.5)
ADI-R (C) Comm Nonverbal	M(SD)	6.1(2.2)	5.3(2.5)	5.5(2.5)	4.2(2.7)	3.6(2.6)	1.6(1.7)	4.3(2.7)	2.8(2.8)
ADI-R (C) RRB	M(SD)	4.7(2.3)	4.6(2.2)	3.8(2.4)	3.7(2.5)	2.9(2.4)	3.4(2.6)	3.3(1.9)	3.1(2.3)
ADOS SA	M(SD)	16.9(3.2)	15.4(3.3)	13.8(4.2)	11.6(4.2)	7.4(3.7)	8.3(4.6)	12.2(4.2)	3.0(1.8)
ADOS RRB	M(SD)	4.8(1.8)	5.2(2.1)	3.3(1.8)	4.0(2.1)	2.1(1.5)	2.6(2.0)	3.3(1.9)	1.2(1)
ADOS CSM	M(SD)	8.8(1.7)	8.6(1.3)	6.6(1.3)	6.9(1.4)	3.5(1.7)	5.7(2.5)	7.2(1.9)	2.3(1.1)
Verbal IQ	M(SD)	41.0(25.9)	45.6(29.2)	48.8(27.3)	61.0(35.4)	55.8(20.9)	70.7(28.8)	74.2(24.0)	100.8(19.0)
	RRR (p)	-		*1.63(0.01*)*		*3.09(0.001*)*		*4.83(0.001*)*	
Nonverbal IQ	M(SD)	67.6(23.9)	64.9(29.4)	74.6(23.7)	73.4(31.1)	75.1(23.6)	81.2(32.0)	88.1(15.7)	100.3(18.4)
	RRR (p)	-		*0.99(0.94)*		*0.70(0.27)*		*0.91(0.80)*	
Gender	Female	17.3%		23.8%		10.0%		8.7%	
	RRR (p)	-		*1.52(0.17)*		*0.51(0.31)*		*0.45(0.33)*	
Race	Minority	20.5%		23.8%		26.7%		8.7%	
	RRR (p)	-		*1.53(0.16)*		*2.14(0.12)*		*0.83(0.82)*	
Final Diagnosis (% observed in each class)	Autism (N=230)	137 (88%)		83 (64%)		9 (30%)		1 (4%)	
	PDDNOS (N=102)	19 (12%)		47 (36%)		18 (60%)		18 (78%)	
	Non-ASD (N=7)	-		-		3 (10%)		4 (18%)	
	N by class	156		130		30		23	

Note. M=Mean; SD=Standard Deviations; First=Data at Initial Assessment; Last=Data at Final Assessment; ADI-R (C) = Current ADI-R algorithm scores on items comparable across ages 2 through 15, summed within ADI-R domains; ADOS SA=ADOS Social Affect domain raw total; ADOS RRB=ADOS Restricted Repetitive Behavior domain raw total; ADOS CSM=ADOS Calibrated Severity Metric score; RRR=Relative risk ratio; p=p-value with 16 degrees of freedom; *p<.01. Results of multinomial logistic regression are in italics, with reference group = Class 1, Persistent High.

Figure 3.1. ADOS Severity Score Latent Trajectory Classes



Note. Y-axis denotes Autism Diagnostic Observation Schedule (ADOS) calibrated severity scores (1-10).

Figure 3.2. Verbal IQ Trajectories by Latent Severity Class

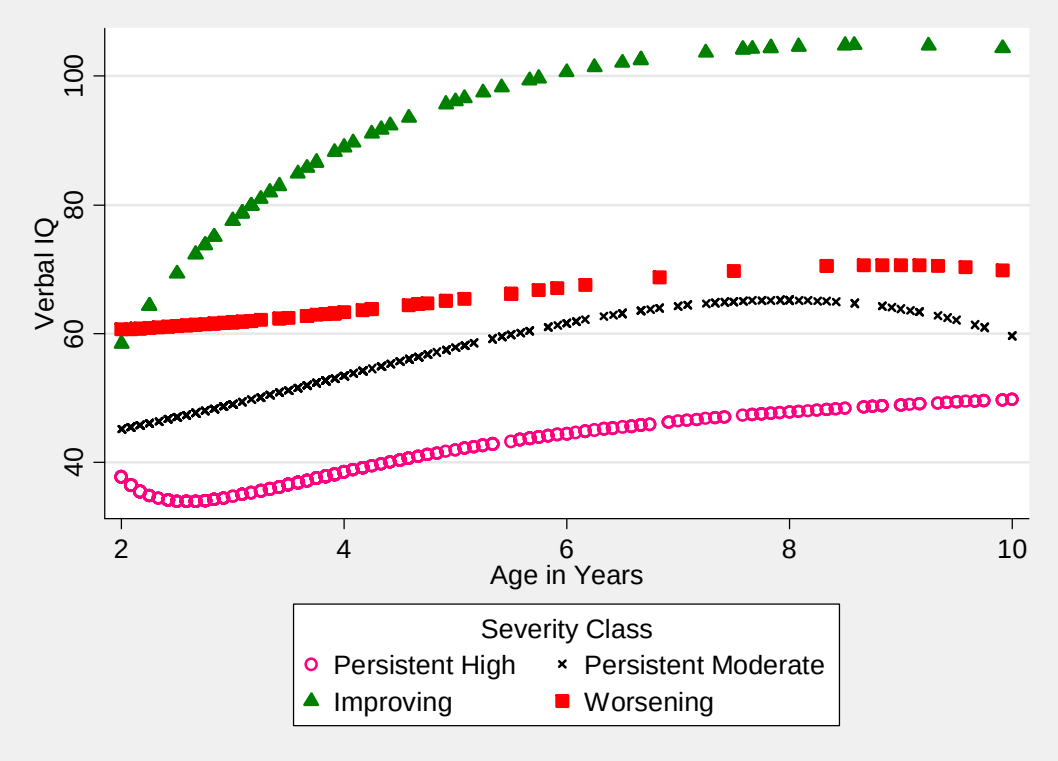
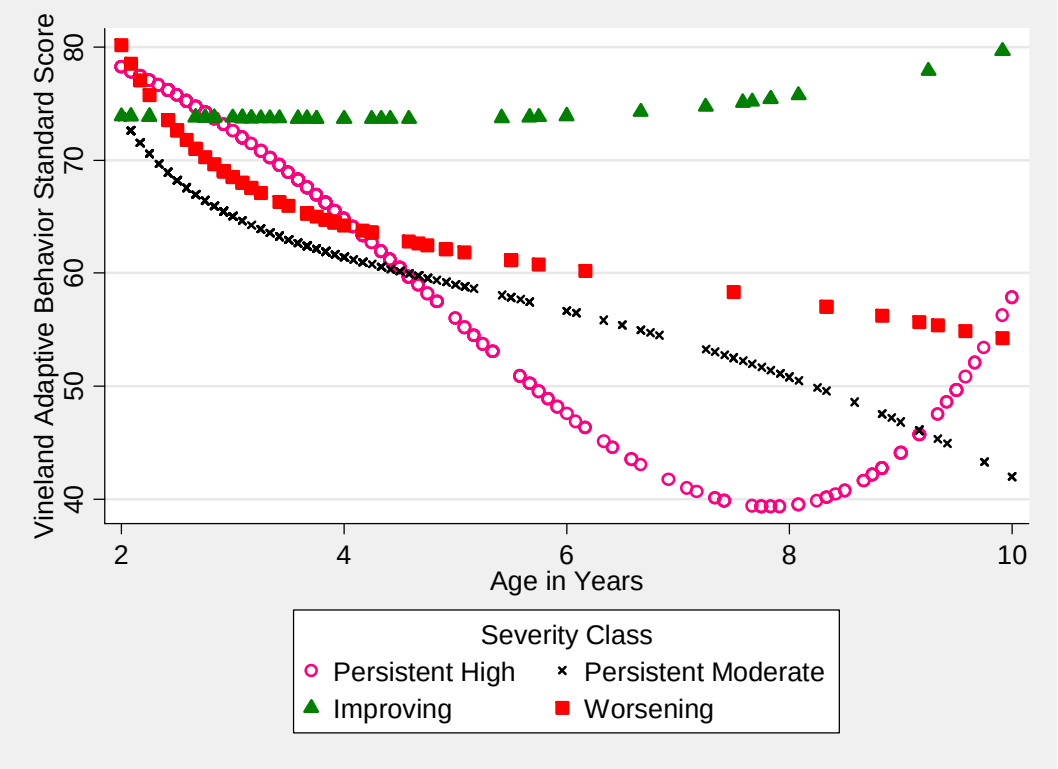


Figure 3.3. Vineland Adaptive Behavior Scales “Daily Living” V-scores by Latent Class



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Chapter IV

Effects of Insight and Social Participation on Depressive Symptoms in ASD

Depression is a pervasive public health concern affecting over 5% of adults in the U.S. at any one time and almost 16% across lifetimes (CDC, 2008). The disorder is associated with physical morbidity and consumes a great deal of health care resources (Greenberg et al., 2003). Loneliness and lack of social connectedness have been shown to predict depression in typically developing populations (Williams & Galliher, 2006; Cacioppo, Hughes, Waite, Hawkley, & Thisted, 2006). Behavioral characteristics that lead individuals to be regarded as odd or different may lead to rejection, loneliness, and poor self-esteem (Sletta, Valas, & Skaalvik, 1996), in turn placing such individuals at increased risk for depression. Individuals with social impairments like those common to autism spectrum disorders, then, are likely at elevated risk for this disabling disorder.

Autism spectrum disorders (ASD) include diagnoses of autism, Asperger syndrome, and Pervasive Developmental Disorder – Not Otherwise Specified. An ASD significantly impedes an individual's ability to negotiate reciprocal social interactions (Howlin, Goode, Hutton, & Rutter, 2004; Lord et al., 2000). Perhaps for this reason, ASD has been linked to depression historically. A child described in Kanner's original observation of autism had a tendency to lapse into a "momentary fit of depression" (Kanner, 1943). Children described by Asperger (1944) had features that raise the possibility of disrupted mood, such as irritability and blunted affect.

Prevalence of depression in ASD

Though depressive symptoms are not a central or specific feature of ASD, more rigorous study of depression in this population is necessitated by prevalence estimates. Although population-based studies of psychiatric comorbidity in ASD have not been undertaken, there is evidence from clinic-based and community studies that depression and anxiety disorders are common across the lifespan (Howlin, 2000; Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Leyfer et al., 2006). Prevalence estimates vary, with reported rates of 10% (Leyfer et al., 2006), 17% (Kim et al., 2000), 30% (Wing, 1981), 37% (Ghaziuddin, Weidmer-Mikhail, & Ghaziuddin, 1998), 41% (Howlin, 2000), and 58% (Lainhart, 1999). Stewart and colleagues (2006) summarized depression as occurring in 4 – 34% of ASD samples they reviewed, a range encompassing much higher rates than those in the general population. Brereton and colleagues (2006) found that depressive symptoms were significantly higher in their sample of 381 individuals with ASD (aged 4-24) versus 550 similarly-aged individuals with Intellectual Disability, indicating that developmental disability alone might not account for the high prevalence of these comorbid symptoms in the ASD population.

Many studies have replicated the existence of a large subgroup within the autism spectrum that has a high incidence of familial mood disorders (documented prior to the birth of a child with special needs), suggesting the two families of disorders are related clinically and genetically (DeLong, 2004). Continued research on depression in ASD is crucial in order to draw comparisons between brain structure and function in individuals with these disorders and to account for high rates of prevalence and heritability. Related

findings should impact our ability to improve quality of life in individuals who suffer with both types of disorders.

Presentation of depression in ASD

Characteristics of autism can complicate observation of, and eventual diagnosis based on, depressive symptoms. A number of typical symptoms of depression to the general population have been identified in cases with comorbid ASD, including notably decreased self care (Clarke, Baxter, Perry, & Prasher, 1999; Wing, 1981), loss of interest in activities (Clarke, Littlehouse, Corbett, & Joseph, 1989; Gillberg, 1985), and psychomotor retardation (Ghaziuddin & Tsai, 1991). Other common symptoms of depression, such as those related to appetite, sleep, communication of affect through facial expression or intonation, and ability to concentrate, are easily masked by pre-existing symptoms of autism (Stewart et al., 2006). Feelings of worthlessness or guilt are not frequently reported in the ASD population (Stewart et al., 2006), perhaps due in part to difficulties with self-report (discussed later). Informal case studies provide a limited number of reports of suicidal behavior, primarily in adults with ASD as opposed to more narrowly defined autism (Ghaziuddin, 2005; Wachtel, Griffin, & Reti, 2010). Ghaziuddin indexes possible depressive symptoms *specific* to or more common in ASD, such as irritability, increase in social withdrawal beyond what is normal for that individual, a change in the character of obsessions (with fixations taking on a more morbid tone), and an increase in compulsive behavior (Ghaziuddin, 2005).

The presentation of depression in ASD also depends on age, level of intelligence, and level of verbal skills. While depression or depressive symptoms can occur across the entire autism spectrum (Stewart et al., 2006), individuals who have more verbal skills or

milder ASD symptoms seem to be either particularly affected or more easily identified (Cederlund, Hagberg, & Gillberg, 2009; Hurtig et al., 2009). Many standard diagnostic measures require verbal self-report and rely on both the insight to recognize symptoms and the verbal aptitude to describe them. Thus, more able ASD clients can better report a history of depressed mood and loss of interest in previously enjoyed activities. In their sample of 46 individuals with ASD aged 18 to 44, Sterling and colleagues found that the 43% of participants who endorsed significant levels of past or current depressive symptoms tended to have higher cognitive abilities and less social impairment (as measured by the Autism Diagnostic Observation Schedule; Lord et al., 2000) than did the overall sample (Sterling, Dawson, Estes, & Greenson, 2008). Several other authors have noted that depression was the most common co-occurring disorder in adolescent and adult samples with Asperger syndrome (n=35; Ghaziuddin et al., 1998) and other more able autism spectrum diagnoses (MA-ASD; N=74 from 8 studies; Howlin, 2000). Even then, the incidence of depression is thought to be underreported in MA-ASD (Ghaziuddin, Ghaziuddin, & Greden, 2002).

Risk factors for depression in ASD

Higher depression rates in the More Able ASD population usually are linked to better verbal self-report ability as discussed above. Alternatively, Ghaziuddin et al. speculated that individuals with greater cognitive ability may in fact be more likely to suffer from depression than others with ASD due to greater awareness of their social deficits and greater desire for social connection (Ghaziuddin et al., 2002). Studies of individuals with schizophrenia have found that greater insight into one's diagnosis and impairments is related to higher rates of depression (Mutsatsa et al., 2006). In a sample of

22 children with ASD aged 7-13, Vickerstaff and colleagues noted that higher chronological age and IQ was associated with higher levels of insight into social skill impairments, and that low perceived social competence was associated with higher levels of depressive symptoms (Vickerstaff, Heriot, Wong, Lopes, & Dossetor, 2007). Previous research suggests both that the desire for social relations increases markedly in many individuals with ASD by adolescence and early adulthood (McGovern & Sigman, 2005), and simultaneously, individuals develop heightened awareness of social isolation within this age period (Ghaziuddin, Alessi & Greden, 1995). It is not surprising, then, that depression in autism also tends to increase with age (Cederlund et al, 2009; Vickerstaff et al., 2007). Thus, while higher verbal and/or cognitive abilities are associated with many positive outcomes (e.g., better academic achievement), they are not necessarily protective of the emotional well-being of people with ASD.

Adolescents and adults seem to be at particular risk, with reports of elevated rates of loneliness (Lasgaard, Nielsen, Eriksen, & Goossens, 2010; Bauminger & Kasari, 2000) and self-perception of low peer approval and high social incompetence (Hedley & Young, 2006; Williamson, Craig, & Slinger, 2008) compared to typical peers. Although several studies have reported that a significant minority of more able young adults and adolescents with ASD have friends (Bauminger & Kasari, 2000; Baron-Cohen & Wheelwright, 2003), findings unanimously suggest that there are differences in both the number and quality of these relationships (Bauminger & Shulman, 2003). Howlin and colleagues (2004) reported that, of 21 to 48-year-olds with ASD, about one-quarter reported having only one friendship with some intimacy and shared enjoyment, and more than half reported having no friendship-like relationships at all.

Anxiety is another potential link between ASD and depression. Though there are few systematic investigations, Lainhart's review (1999) states that up to 84 % of children and adults with autism are reported to have at least one type of anxiety (e.g., social anxiety, separation anxiety). She notes that anxiety is so common in ASD that a separate diagnosis of an anxiety disorder often is not given, even in the face of very obvious and impairing symptoms. Clinical levels of anxiety are especially common in the MA-ASD population, again attributed to increased awareness of impairment (Howlin, 2000; Kim et al., 2000; Lainhart, 1999; Tantam, 1991). Anxiety is likely associated with depression within ASD as has been established in the general population (Gaynes et al., 1999). Therefore we will collect data on anxiety symptoms in our sample, though we focus on depressive symptoms as the primary outcome within this dissertation project.

Challenges in assessing depression in ASD

Despite the pressing need for research into ASD and comorbid depression, progress is complicated by obstacles to assessing depressive symptoms in individuals with ASD. Assessment of most depression criteria in the general population relies on communication skills often absent or abnormal in ASD. Additionally, even those with relatively well-developed language often have difficulty expressing feeling or mood states and fail to use abstract concepts or metaphors (Perry, Marston, Hinder, Munden, & Roy, 2001). Individuals on the autism spectrum tend to perceive, remember, and interpret both social and nonsocial information differently, and often exhibit limited insight and perspective-taking skill (Johnson, Filliter, & Murphy, 2009; Hedley & Young, 2006; Stewart et al., 2006; Beebe & Risi, 2003; Blackshaw, Kinderman, Hare & Hatton, 2001; Hare, 1997). In a 2004 paper by Hill, Berthoz, and Frith, 27 adults with high-functioning

autism, or HFA (i.e., ASD and IQ>70), had much more difficulty identifying and describing feelings, and had more externally oriented thinking, than did 35 adult controls and 47 ASD family members. Almost 85% of the ASD group fell in the slightly or severely impaired ranges on the Toronto Alexithymia Scale, a questionnaire that operationalizes deficiency in understanding, processing, and/or describing emotions, whereas 79-83% of the control groups fell in the nonimpaired range on this measure.

Validity of depression diagnosis likely is compromised when individuals with ASD do not have sufficient ability to communicate about abstractions in order to describe their internal states (Costello, Egger, & Angold, 2005). Despite the implied difficulty of reporting on their feelings, however, the ASD group in the Hill et al. sample endorsed high levels of depressive symptoms on the Beck Depression Inventory (BDI-II; Beck, 1996), with 75% meeting clinical cut-offs for depressive concern versus 27% of the relatives and 17% of the typical controls. In a 2009 study by Cederlund and colleagues, scores on the Beck Depression Inventory (BDI) were consistent with clinical diagnoses of depression in a sample of 76 young men with Asperger syndrome. This is a promising start, though validation studies of commonly used depression inventories and interviews are needed in ASD samples.

Treatment

Families and clinicians clearly acknowledge the need for depression treatment for individuals with ASD. One indication of this is the very high rate of psychotropic medication use in the ASD population (Esbensen, Greenberg, Seltzer, Aman, 2009; Aman, Lam, & Collier-Crespin, 2003). Though in many cases selective serotonin reuptake inhibitors (SSRIs) are prescribed in an attempt to reduce repetitive behavior or

anxiety over insistence on sameness in routines, this family of drugs also is used commonly for the purpose of treating depressive symptoms in adolescents and adults with ASD. Reportedly over 50% of individuals with MA-ASD take such medication for the purpose of treating mood and anxiety disorders (Ghaziuddin et al., 2002). Despite its prevalent use, few if any randomized controlled studies exist exploring the effectiveness of psychotropic medication in treating depressive disorders in individuals with ASD (Gerhard, Chavez, Olfsun, & Crystral, 2009).

Young people with MA-ASD have been supported in achieving better outcomes in terms of employment and partial independence than were observed in previous decades (Howlin et al., 2004); it is ironic that, by including individuals with ASD in the community and helping them to develop more insight into the social world, we may perhaps be increasing their risk for depressive symptoms. The field of autism research and clinical work has an important challenge ahead to support positive outcomes in the mental health, well-being, and social networks of these individuals, in addition to continuing to build opportunities for independent living and jobs. Fortunately, interventions to improve social contact and support networks are becoming more well-established (e.g., Laugeson, Frankel, Mogil, & Dillon, 2009). With adequate study of the *social mechanisms* contributing to or protecting against depressive symptoms in ASD, we may find evidence of the need for relatively simple treatments to complement or reduce the need for multiple medications to address depression in ASD.

Psychosocial pathways to depression in ASD

The purpose of this project is to examine psychosocial mechanisms that may impact the development of depression in adolescents and adults with MA-ASD. To our

knowledge, no previous studies have examined the direct relationship between insight into social deficits or unfulfilled desire for social contact with depressive symptoms in this population. Specifically, we want to test (1) whether greater awareness of one's own social impairments is associated with higher levels of depressive symptoms, and (2) whether a disparity between social interest and social participation predicts higher levels of depressive symptoms in this population. We would expect that participants with ASD will tend to endorse fewer autism symptoms and rate these symptoms as less impairing than will professionals/caregivers. However, we hypothesize that *participants with higher levels of insight into their ASD symptoms will report higher levels of depressive symptoms*. We also plan to examine whether level of social participation moderates the relationship between insight into ASD symptoms and self- and caregiver-ratings of depressive symptoms. We hypothesize that *a profile in which social motivation is higher than social participation will be associated with higher levels of depressive symptoms*.

The study of comorbid depression in ASD has been hindered by a lack of appropriate measures and the inherent difficulty in recognizing psychiatric symptoms in individuals who also have impairments in language, cognitive functioning, communication of affect, and insight (Leyfer et al., 2006). To ensure a reasonably limited scope, this project focuses on "depressive symptoms" as an outcome measure, rather than on clinical diagnoses of depressive disorders. Measurement issues reviewed above apply to the symptoms as well as the disorder. In the absence of depression measures that have been validated in the ASD population, we will use the BDI as the outcome measure in this study.

Methods

Participants

Data were collected from a sample of 46 adolescents and adults with autism spectrum disorders. Inclusion criteria included (1) chronological age between 15 years, 0 months and 35 years, 11 months, (2) a verbal IQ of 70 or greater, (3) reading comprehension at the fifth-grade level or beyond, (4) a clinical diagnosis of an ASD, including Autistic Disorder (i.e., autism), Asperger syndrome, and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), and (5) the willingness of a parent/caregiver who was familiar with the participant as a young child to participate as well. Exclusion criteria included significant sensory or motor impairment (e.g., blindness, severe cerebral palsy) that would preclude completion of the standard assessment battery, as well as acute psychiatric disorder (e.g., schizophrenia).

Participants ranged in age from 15 to 31 years old. Families were recruited from recent clinic or research participants at the University of Michigan Autism and Communication Disorders Center (UMACC) who consented to be re-contacted for future research (n=14, including 9 former UMACC social group members), those currently participating in UMACC adult or "teen" social groups (n=5), 21 individuals participating in the "Longitudinal Studies of Autism Spectrum Disorders: 2 to 22," a NIMH-funded research project currently ongoing at UMACC, as well as 6 participants who responded to public recruitment for this project in the southern Michigan area. Community recruitment strategies included sending flyers and making presentations at ASD resource centers, social groups, or job-coaching groups. Longitudinal study probands were

consecutive ASD referrals at age 2 to clinics in North Carolina and the Chicago metropolitan area (Lord et al., 2006); they have been seen at ages 2, 3, 5 and 9 years and now range in age from 16-22 years. These participants had face-to-face assessments conducted by researchers traveling from UMACC to North Carolina, Chicago, or new locations to which the families have moved. The rest of the sample was seen at the UMACC clinic or in their homes in Michigan.

An additional 26 participants were recruited, consented, assessed, and given monetary incentives, however their data were excluded from this sample due to verbal IQ below 70 (n=9), probable diagnoses of Bipolar disorder in addition to previously diagnosed ASD (n=2), or failure to meet criteria for a best estimate clinical diagnosis of an ASD (n=14), as well as one eligible participant who chose not to answer a significant number of items and measures within the research protocol, rendering her data unusable due to missing values. Table 4.1 outlines recruitment and participation details of this sample.

Mean chronological age in the sample was 20 years, 10 months (SD=5 years). Mean verbal IQ was 106 (SD=15.7) and nonverbal IQ was 104 (SD=15.7). Data were available from 5 females (11% of the sample). Race and ethnicity of the sample included 78% Caucasian, 11% African American, 5% with two or more racial affiliations, and one person (2%) each from the Asian, American Indian, and "Other" categories. The majority of the sample (73%) currently was living at home with one or both parents, 12% lived in college or university housing, 5% lived on their own with significant in-home professional assistance, 4% lived on their own with relative or complete independence, and 7% did not provide information about their living situation. Participant education

varied as follows: 31% of the sample was currently in high school receiving significant services, 27% was in high school with minimal to no special education services, 32% had attempted some college or was currently in college, 3% had completed a college degree, and 7% did not provide information on their educational level. Maternal education ranged from 28% with graduate education, 24% who completed Bachelor's degrees, 29% with some college, 5% high school graduates, and 2% who had completed 9th grade, with data not provided for one participant. See Table 4.2 for a more detailed description of this sample, and Table 4.3 for information on parent/caregiver participants.

Best estimate clinical diagnoses of autism, based on clinical judgment informed by diagnostic measures referenced later, were assigned to 20 individuals (43%), PDD-NOS diagnoses were made in 21 participants (46%), and 5 (11%) had Asperger syndrome. In addition to a diagnosis on the autism spectrum, 5 individuals received a diagnosis of an anxiety disorder (n=2 with Generalized Anxiety Disorder and n=3 with Anxiety Disorder, Not Otherwise Specified; 11% of the sample) and 8 participants received a diagnosis of a depressive disorder (6 with Recurrent Major Depressive Disorder, 1 with a single current episode of MDD, and 1 with Dysthymic Disorder; 17% of sample). Procedures regarding diagnostic decision-making are included in the next section.

Procedures

The data collection protocol included a packet of questionnaires and a face-to-face assessment for both the adolescent or adult participant with ASD (i.e., proband) and his/her parent or childhood caregiver (because no non-parent caregivers participated in this sample, we will refer to "parent" participants from this point on). The estimated time

to complete the mailed questionnaire packets was approximately 20 minutes for probands and 15 minutes for parents. Face-to-face assessments took approximately 3 hours for probands and 4 hours for parents. Some measures used solely to confirm ASD diagnoses were not re-administered for those participants who previously had received an ASD diagnosis from UMACC. Participants received $50 for the proband session and $50 for the parent session; both probands and parents received gift cards dependent on their own participation only. For participants in the Longitudinal Study, incentives for full participation included gift cards of $50 as well as brief reports on the assessment results. Additional measures were added to the Longitudinal protocol for these participants. All research participants had access to extended fee-for-service clinical services through UMACC, with financial assistance offered as needed.

Data were collected and clinical diagnoses assigned by graduate students in the University of Michigan clinical psychology doctoral program and UMACC research assistants, all of whom had undergone extensive training to achieve research reliability on the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) and the Autism Diagnostic Interview-Revised (ADI-R; Rutter, LeCouteur, & Lord, 2003). Examiners had a minimum of two years' experience assessing individuals with ASD and making autism spectrum diagnoses. In some cases, different research examiners assessed the proband and parent participants; both examiners discussed the case and came to a consensus agreement about clinical diagnoses (both in regard to the autism spectrum diagnosis and relevant other mental health conditions) based on all available information, including standardized rating instruments and a brief unstructured clinical interview (see Table 4.4 for a list of measures taken into account in making clinical diagnoses).

A risk management protocol for this study included assessment of suicidal ideation, seeking of supervision from a licensed clinical psychologist, and arrangements to transport participants to the nearest hospital Emergency Department if necessary. Steps 1 and 2 of this plan occurred in two cases, and these participants received follow-up services from both UMACC and local mental health resources. All individuals given a diagnosis of a mood disorder through this study received clinical feedback and recommendations, except in the case of one individual whose disorder was already known to his family and who was receiving psychiatric care. The University of Michigan Institutional Review Board in Health and Behavioral Sciences approved all procedures related to this study.

Measures

Proband measures

The standard battery for participants with ASD was as follows: in the mailed packets, probands received informed consent documents and a demographic questionnaire, along with a number of questionnaires pertaining to psychological health (see Table 4.4 for a complete list of the assessment protocol). During the face-to-face assessment, probands completed the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) for a measure of cognitive ability; the Neale Analysis of Reading Ability (Neale, 1997) or the Wide Range Achievement Test (WRAT; Wilkinson & Robertson, 2006) reading comprehension subtests in order to verify reading comprehension necessary to complete questionnaires; the ADOS to confirm diagnosis; a brief close-ended interview on depressive symptoms intended for populations with developmental delays, the Self-Report Depression Questionnaire (SRDQ; Reynolds &

Baker, 1988); the Beck Depression Inventory (BDI-II; Beck, 1996) or Child Depression Inventory (CDI; Kovacs, 1992) depending on age; and an adapted version of the Social Support Questionnaire (SSQ; Sarason, Sarason, Shearling, & Pierce, 1987).

The Behavioral Perception Inventory (BPI)

In addition to the instruments above, participants completed two new measures created specifically for our variables of interest. The first is the Behavioral Perception Inventory (BPI), on which participants rate to what degree each of 34 autism-related symptoms and positively-worded "filler" items describes their own behavior (Part A), and to what degree others think the behavior in question applies to the participant (Part B). Responses are in the form of two distinct four-point Likert scales for self-ratings in Part A of each item (*Almost Never, A Little, Pretty Much, Almost Always*) and ratings of others' perception of one's own behavior (e.g., *"How much do others think you…* [do the behavior in question]") in Part B (*Not Much, A Little, Pretty Much, Very Much*). The BPI contains 3 sets of questions that are asked twice throughout the measure, once with positive wording (e.g., "Do you remember to ask others about their interests and experiences") and once with negative wording (e.g., "Do you forget to ask others about their interests and experiences?"). These question pairs are intended to function as a validity scale, allowing data to be excluded for those who rate themselves highly inconsistently on the same concept or when the question is reframed in a positive or negative direction.

After the proband assessment, a clinician-rated version of the BPI was completed by the examiner, who rated the proband on the same items and using the same scale as did the proband him or herself. Parents also filled out a parent-version of the BPI about

their children. See Appendix A of this chapter for proband-, clinician-, and parent-rated versions of the BPI.

The Social Interests and Habits Questionnaire

The second new measure created for this study was the Social Interests and Habits Questionnaire (SIH; see Appendix B), which assesses participants' wish for involvement in several social domains as well as their current degree of involvement. The "Social Current" section (SIH-SC) includes 7 questions about social participatory behaviors rated on a four-point likert scale (*None, A Little, Pretty Much, A Lot*) and 6 qualitative questions about the proband's current social participation (e.g., *"If you do have a job now, what do you do at your job?"*). The "Social Wishes" section (SIH-SW) includes 7 similar, Likert-rated questions about the proband's desire for the same social participatory behaviors, as well as 4 additional Likert-rated questions and 4 write-in response questions that address desire for the social behaviors measured qualitatively on the SIH-SC (e.g., *"If you got a first job or a new job someday, what kind of job would you want?"*). The SIH includes a final section ("Social-Others," SIH-SO) with 7 Likert-rated questions that ask the proband to rate the social practices of other people his/her age, in order to assess for response patterns biased by social desirability effects. The SIH was counter-balanced such that a random half of participants rated their desired amount of social experiences (SIH-SW) before answering questions about their actual amount of current social contact (SIH-SC), with the other half of participants receiving the 'current' questions before the 'desired' questions. The SIH-SO was always given last. Only the first seven questions of the SIH-SC and -SW were used in these analyses, thus excluding the qualitative questions at this point.

The proband battery was structured to avoid bias or contamination of responses. In addition to the counter-balancing of the SIH, the self-report depression measures (SRDQ and BDI) were administered directly following the cognitive test, before the ADOS, BPI, or measures of social experiences and support, in order to eliminate a priming effect of potentially negative topics.

Parent measures

Parent participants received a mailed packet containing consent forms (and permission forms for those with participating children under 18), as well as a background history form and a number of questionnaires regarding their child's emotional health. See Table 4.4 for a complete list of parent-rated instruments. During the face-to-face assessment, parents completed the Autism Diagnostic Interview-Revised (ADI-R; Rutter, LeCouteur, & Lord, 2003) in order to confirm diagnosis; the second edition of the Vineland Adaptive Behavior Scales (Sparrow, Cicchetti, & Balla, 2005) to assess adaptive functioning of the participant; an interview on the proband's depressive symptoms adapted for use in both adolescents and adults, the Children's Depression Rating Scale (CDRS; Poznanski & Mokros, 1996); and a brief interview about mental health history of the proband's immediate and extended family. Parents also completed the parent version of the BPI, on which they rated the adolescent/adult participants' behavior for the same symptoms and on the same scale as those rated by the proband him/herself (see Appendix A).

Statistical analysis

As the measures used to operationalize the two main hypotheses of this study were newly created for that purpose, Cronbach's alpha coefficient was used to measure

internal consistency within the BPI and the SIH. Correlations were generated between new measure items and participant age and verbal IQ to assess the effects of these participant characteristics on item responses.

To address the first hypothesis, that higher insight into one's autism symptoms will predict greater levels of depressive symptoms, raw totals of Proband BPI scores and Examiner BPI scores were entered into a multiple linear regression model, along with chronological age centered at the sample mean, as predictors of Beck Depression Inventory scores. The interaction between Proband and Examiner BPI scores as a predictor of BDI scores could not be assessed due to multicollinearity between raters' BPI totals. See the end of this section for information on meeting assumptions for this and all other regression analyses described herein.

Next, exploratory methods were used in an attempt to make inferences about particular symptom groupings in which differing levels of insight might influence depression scores. BPI scores were compared across participants, parents, and examiners to operationalize level of symptom-related insight for each individual. Bivariate correlations were generated for each differently-rated item pair (e.g., Parent BPI Item 3 and Examiner BPI Item 3) in order to make a decision about whether to combine the measures into the standard BPI rating to which the proband's own ratings would be compared; consistent correlation at or above r=.70 was chosen as the criterion for combining information from both raters. Correlations between Examiner and Parent ratings generally failed to meet this criterion, so BPI-Examiner ratings were used alone as the comparison to the Proband ratings. The difference between Examiner and Proband ratings (e.g., BPI Item 2, Part A: Examiner Rating=3 and Proband Rating=1; 3 – 1 yields

a difference score of 2) were generated to assess item-level patterns of awareness of symptoms (e.g., strong Examiner-Proband agreement), lack of insight (e.g., Examiner rates symptom as more impairing than does Proband), or oversensitivity (e.g., Proband rates symptom as more impairing than does Examiner). Examiner-Proband difference scores for each of 25 items (excluding positive "filler" items) were then entered into an exploratory factor analysis (EFA) model to examine the correlation structure of the 25 difference items.

Standardized factor scores from the EFA were entered into a multiple linear regression model, along with standardized chronological age and verbal IQ covariates, as predictors of continuous depression scores on the BDI. Insight factor scores and age and verbal IQ covariates were also entered into logistic regression models as predictors of clinical diagnosis of a mood disorder (with a binary rating 0='No Depressive Disorder' and 1='Depressive Disorder Present'). Linear regression was used to further examine whether adaptive behavior skills predict depressive symptoms, and if so, whether they mediated the impact of insight into functional independence. The same analyses were undertaken separately for Part A (Proband's rating of own behavior) and Part B (Proband rates the degree to which *other people* think the behavior applies to him or herself), or the corresponding Examiner-Proband difference scores, for each BPI question.

To address the second hypothesis, in which a disparity between social interest and social participation will be associated with higher depressive symptoms, exploratory factor analyses were conducted separately for SIH-Social Current items and SIH-Social Wishes items. Linear regression (with dependent variable=BDI scores) and logistic regression (with dependent variable=clinical diagnosis of depression) with age and verbal

IQ covariates were used to assess each extracted SIH factor score independently, as well as interactions between the "Social Currrent" and "Social Wishes" factors, as predictors of these outcomes. To explore these results further, a subdomain total from the ADI-R algorithm that quantifies parent report of shared enjoyment behaviors at age 4-5 was used to represent a pre-depression retrospective report of proband social interest (i.e., as an alternative indicator of social interest that was not measured simultaneously to the BDI); this score was entered into a regression model as a predictor of BDI scores, controlling for age.

For all regression models described above, tolerance and variance inflation factor (VIF) statistics were checked for evidence of multicollinearity; criteria for concern were tolerance scores less than 0.2 and mean VIF greater than 1. Standardized residuals were plotted against standardized predicted values, and partial plots were also examined for evidence of violations of homogeneity of variance and linearity. Standardized residual histograms and normal probability plots were assessed for indications of normal distributions in the variables of interest. Cook's Distances were checked for scores greater than 1 to draw attention to single cases that may have had undue influence on the models.

Results

The entire sample of 46 individuals was used in analyses related to the Social Interests and Habits Questionnaire. Data from 7 participants were excluded from analyses of the Behavioral Perception Inventory based on validity checks embedded in the measure. BPI data were excluded from those individuals (Age Range=16-20 years, M=19

years, SD=1.7; Verbal IQ Range=72-126; M=98, SD=22) whose responses varied over 3 points on the Likert scale on any one of 3 conceptually-identical pairs of questions, as well as those whose responses varied at least 2 points on two or more on the question pairs. This brought the sample size to 39 for analyses of the BPI.

For all versions of the BPI, positively-worded items were reverse-coded such that increasing scores denote increasing ASD symptomatology ratings. Further, "filler" items intended to make the questionnaire a more positive experience for participants (e.g., "*Do you spend time doing things you enjoy, like reading or watching TV?*") were excluded from BPI analyses, leaving an item set of 28.

For each regression model described below, assumptions were met for adequate use of these analyses, with the exception of a model including Proband BPI total, Examiner BPI total, and an interaction term for both. In this one case, tolerance scores ranged from 0.01 to 0.03 and variance inflation factor (VIF) statistics from 29.4 to 81.7, indicating serious concern about multicollinearity between the predictors; this analysis was not interpreted or reported. For all other regression analyses, tolerance scores were around 0.8-0.9 and VIF statistics were around 1 on average, indicating no concern about multicollinearity between model predictors. No evidence of violations of homogeneity of variance and linearity were noted in the plots of standardized residuals by standardized predicted values or partial plots, with the exception of Z-scores based on chronological age, which showed evidence of possible heteroscedasticity (i.e., unequal variance of residuals). Standardized residual histograms and normal probability plots indicated normal distributions of the variables of interest. Cook's Distances were all well below 1, indicating that no single case had undue influence on the models.

Instrument development

Internal consistency

Internal consistency of the new measures was assessed with Cronbach's alpha coefficient (Cronbach, 1951). Alphas on the BPI were highest for Examiner (0.92) and Caregiver (0.90) versions, and lowest, though still acceptable, for the Proband Rating Others' Perceptions (Part B of each Proband-rated item), at 0.86. Cronbach's alphas for the SIH were somewhat lower, at 0.64 for the SIH-Social Current scale items and 0.58 for the SIH-Social Wishes scale. Though this falls below satisfactory levels (.70 is generally accepted as such; Streiner & Norman, 2003), a low number of items tends to deflate Cronbach's alpha coefficient spuriously, and only 7 items were included in the SIH analyses. It is also possible that uncorrelated latent factors (e.g., two possibilities were 'desire to spend time doing hobbies alone' and 'desire to spend time outside of the house or with friends') exist in this measure, with potentially larger alpha coefficients within factors.

Correlation with age and verbal IQ

Item correlations with chronological age and verbal IQ were also reviewed in order to examine the independence of the measures from these participant characteristics. The BPI-Caregiver had no items correlated above r=.30 with either age or verbal IQ. For the BPI-Examiner, two items correlated with chronological age beyond r=.30 ("*When [proband] sets long-term goals, they are realistic*" at r=.47, p<.01, and "*[Proband] does things that are rude or inappropriate even when he/she doesn't mean to*" at r=-.33, p=.05) and one item correlated with Verbal IQ beyond r=.30 ("*It is easy for [proband] to keep a conversation going*" at r=-.43, p<.01). For the BPI-Proband, three items correlated

with chronological age above r=.30 (Items 14, 16, and 33), though none above r=.35, and three items correlated with Verbal IQ above r=.30 (Items 10, 22, and 29), though none above an absolute value of .45.

All SIH-SC and SIH-SW items were correlated with chronological age and verbal IQ at no more than r=.30 with the exception of "*How often would you want to spend time with family members?"* (SIH-SW Item 1; r=-0.40 with Chronological Age, p<.01) and "*How often do you chat online with friends*?" (Item 4 on SIH-SC Item 4; r=.34 with Verbal IQ, p<.05). None of the significant correlations between new measure items and age or IQ were judged to be high or concerning, especially as both characteristics would be controlled for in regression analyses.

Behavioral Perception Inventory totals as predictors of depressive symptoms

Because of the small sample size for BPI analyses (n=39), only 3 or fewer parameters could be estimated in linear regression models (Harrell, 2001). Initially, chronological age and verbal IQ variables were centered at the sample mean and entered into a multiple linear regression model as sole predictors of Beck Depression Inventory scores, in order to assess the effects of these participant characteristics on depression. These predictors explained only 12% of the model variance, and the overall model $F(2,36)=2.4$ failed to reach significance. Verbal IQ had no significant association with BDI scores in this model, but age was significant at the p<.05 level (B=2.6; $\beta = .34$, p=.04). No particular pattern emerged between chronological age and BDI scores in a scatterplot; the two variables were correlated at r=.30 (p<.05), suggesting that higher BDI scores may be somewhat associated with older ages.

The 28 usable, recoded BPI raw item scores were summed for Proband Part A (i.e., Proband Rates Self) ratings and for Examiner BPI ratings. Proband and Examiner BPI totals were entered into a regression model, again with BDI totals as the dependent variable. Standardized chronological age was included as a covariate in the model. Controlling for Examiner BPI totals, Proband-rated BPI totals were highly significant predictors of BDI scores, $B=.44$; $\beta = .59$, $p<.001$. This finding indicates that higher levels of *perceived* autism-related impairment are associated with higher levels of depressive symptoms on the BDI, controlling for actual level of impairment (Examiner-rated BPI total). Standardized age and Proband and Examiner BPI totals were also entered into logistic regression models as predictors of clinical diagnosis of a mood disorder, and none of the three variables was a significant predictor of depressed diagnosis.

Because of multicollinearity in the data, the interaction of Proband and Examiner BPI totals could not be assessed for patterns in depressive symptoms on the BDI. Thus, overall group depression scores could not be compared between individuals with good insight into their actual symptoms (e.g., Proband and Examiner scores both low or both high) and individuals who tend to rate themselves as being more impaired on the BPI due to a "halo effect" of negative cognitions, perhaps as a result of depression (e.g., Examiner BPI scores lower than Proband BPI scores). For this reason, we went on to attempt more exploratory analyses of the relationship between Proband and Examiner BPI scores and BDI scores.

Exploratory analyses of the effects of symptom domain-specific insight

Computing "insight" scores

Bivariate correlations were generated for all items from Caregiver and Examiner versions of the BPI for the purpose of creating a combined standard rating to which probands' own self-ratings would be compared for insight into symptoms. Correlations between the two non-proband versions were lower than expected, and none exceeded the desired cut-point of r=.70. Because many items on the BPI were based on ASD symptoms elicited and scored in the ADOS, the Examiner BPI scores (based on ratings from clinicians who have achieved research reliability on the ADOS) were used as the absolute rating of proband symptomatology.

The difference between Examiner and Proband ratings was generated for each item by subtracting Proband ratings from Examiner ratings after each had been recoded to progress in the same direction (with higher scores indicating greater impairment). On these difference scores, high positive numbers (2 to 3) on Examiner-Proband Difference scores represented symptoms that the examiner rated as more evident in or problematic for the proband than did the proband him or herself. Larger negative numbers (-2 to -3) indicated those symptoms about which probands tended to show possible *oversensitivity*, in that the proband rated him or herself as more impaired on that symptom than did the examiner. Scores of or close to 0 (-1 to 1) indicated strong Examiner-Proband agreement and thus awareness of ASD symptoms on the proband's part.

Exploratory factor analysis of BPI Examiner-Proband differences

Exploratory factor analyses were run including Examiner-Proband Difference scores, Chronological Age, and Verbal IQ. Promax rotation was chosen to allow for

correlation between factors. Communalities (the percentage of variance in a given item explained by all of the factors) were less than 0.50 for fourteen of the 28 Part A items and 10 of the 28 Part B items, indicating a potentially underpowered analysis. Item-to-subject ratio also was quite low (1:1.8), and thus these results may be specific to the current small sample.

Examiner-Proband Rates Self (Part A) Difference scores: Ten factors had eigenvalues above 1.00 and explained 77% of the variance in the model. To maximize interpretability, items were forced to load onto 3 factors (indicated by the scree plot as a good cut point), which explained 42% of the variance (see Table 4.5). The first factor included 8 items pertaining to difficulty making friends (4, 19), conversation (15, 26), and monologue (10, 16, 21, 30), as well as 11 other items (e.g., 11-feels comfortable in social situations). This factor, named "Insight into Conversation/ Monologue," explained 24% of variance in the model. The second factor included 4 items related to insistence on sameness in routine and rituals (2, 9, 23) and noticing or remembering details (3); this was named the "Insight into Compulsive/Ritualized" factor, and it was negatively correlated with Item 14: *Stands too close to others* (i.e., this item had a negative factor loading of -.49). The final factor had two strong loadings, Item 6: *Realistic future goals* and Item 20: *Independent in caring for self*, and one negative loading (28: *Eye contact*). The third factor explained 8% of the variance and was called the "Insight into Functional Independence" factor. The three factors were minimally correlated ($r<.20$).

Examiner-Proband Rates Others' Perception of Self (Part B) Differences scores: Nine factors had eigenvalues above 1.00 and explained 74% of the variance in the model. Part B item difference scores were forced to load onto 4 factors as indicated by the scree

plot, and these first four factors explained 49% of the variance (see Table 4.5). The first factor included 14 items pertaining to comfort with routine, insistence on sameness, hyperfocus, and conversational monologue, as well as stereotyped or odd speech and rude/ inappropriate behavior and interrupting. This factor, though slightly different from the Proband-Rates-Self factor described above, was named the "Insight into Compulsive/Ritualized (B)" factor, and it described 21% of the variance. The second factor, called "Developmental Effects" and describing 11% of the variance, had negative factor loadings for Age and Verbal IQ and included items 20: *Independent in caring for self* and 33: *Hard to keep attention where it's supposed to be*. The third factor explained 9% of the model variance and related to making friends and the ability to read sarcasm and facial expressions (per loadings of 4 items); it was named "Insight into Peer Difficulties." The final factor again had a strong loading for Item 6: *Realistic future goals* (though not Item 20: *Independent in caring for self*). It also included Item 29: *Controls anger and anxiety* and had a negative loading for 28: *Eye contact*. This so-named "Future Goals" factor with these three items explained only 7% of the model variance. However, with a factor loading of .76 for Item 6, the evidence that a four-factor solution met 'best-fit' criteria by eigenvalues and scree plot, and its similarity to the BPI Proband-Rates-Self factor, it was retained as a distinct factor. All four factors had low positive correlations, at or below r=.30.

BPI difference factors as predictors of BDI totals

Multiple linear regression analyses were performed separately for factor scores derived from BPI Part A (Examiner-Proband Rates Self) and Part B (Examiner-Proband Rates Others' Perception of Self) items. Beck Depression Inventory totals were entered

as the dependent variable to examine the effects of ASD symptom awareness (or "insight") on depressive symptoms. Models were run with the three BPI Part A (Proband Rates Self) Difference Factors alone and with standardized age scores included; in both cases, only Factor 3: "Insight into Functional Independence" was a significant predictor of BDI scores (see Table 4.6). Evidenced in scatterplots of these data, greater degrees of agreement between Proband and Examiner ratings, up through Proband ratings of impairment that surpassed the Examiner ratings, were associated with increasing levels of depressive symptoms primarily for Factor 3 scores.

Because a 4-factor solution best fit BPI Part B (Proband rates others' perception) Difference Scores, not all the Part B factors and covariates could be entered in the same regression model due to sample size parameter-constraints. Various combinations of predictors were entered into separate regression models. Neither Part B factor loadings nor standardized age predicted BDI scores at a significant level.

BPI difference factors as predictors of clinical diagnosis

Insight factors and age and verbal IQ covariates were also entered into logistic regression models as predictors of clinical diagnosis of a mood disorder. Interestingly, Part A Examiner-Proband Rates Self Factor 2 ("Insight into Compulsive/Ritualized Behavior") significantly predicted a clinical diagnosis of depression, whether or not standardized age and verbal IQ variables were included in the model, B(SE)=1.5(0.7), p=0.03, Nagelkerke R^2=.45. In this case, individuals who received clinical diagnoses of depressive disorders in this sample (n=8) tended to have *poorer* insight into their compulsive/ritualized behavior. No other factors for either Part A or Part B difference scores, age, or IQ were significant.

Vineland Adaptive Behavior scores as predictors of BDI totals

Results of linear regression models with BPI insight factors as predictors indicated that awareness of impairments in setting realistic goals and caring for one's self independently was associated with depressive symptoms. We next used adaptive behavior scores from the Vineland Adaptive Behavior Scales, 2nd edition, to assess whether *insight into functional independence impairments* or the actual *functional independence impairments* themselves were driving the association between that insight factor and BDI scores. Scatterplots and bivariate correlations indicated that all subdomains of the Vineland-II, including Communication, Daily Living Skills, Socialization domain standard scores, and the Overall Adaptive Behavior Composite standard score (VABCST) were similarly negatively correlated with BDI scores, e.g., VABCST and BDI $r=-.45$, $p<.01$. In other words, better adaptive behavior was associated with less depression. Therefore, only the overall composite score (the VABCST) was entered into a linear regression model predicting BDI totals, again controlling for age and verbal IQ. VABCST approached significance in the model ($B=-0.2$; $\beta=-.37$, $p=.05$), whereas age and IQ did not. However, when centered age, verbal IQ, VABCST, and the "Insight into Functional Independence" factor (Factor 3 of BPI Part A) were entered simultaneously, only the Insight factor was a significant predictor of BDI totals ($B=-3.0$; $\beta=-.34$, $p=.04$). Multicollinearity was not noted in the regression diagnostics, and the standardized score of overall adaptive skills was correlated at 0.19 with factor loadings of insight into functional independence. The actual adaptive behavior score also approached significance ($B=-.2$; $\beta=-.4$, $p=.06$), in the direction of poorer

adaptive behavior scores being associated with higher scores on the BDI, but the degree of impairment itself did not control for the impact of *insight* into adaptive impairments.

Exploratory factor analysis of SIH

In Hypothesis 2, we predicted that a disparity between social interest and social participation as measured by the Social Interests and Habits Questionnaire would be associated with higher depressive symptoms. Exploratory factor analyses were undertaken separately for SIH-Social Current items and SIH-Social Wishes items to first explore the factor structure of this new measure. Again, analyses were run with Promax rotation to allow for correlation between factors. Item-to-subject ratio was 1:6.6, and all communalities were above 0.50, except for age and verbal IQ in the SIH-SW analyses, which indicates that the factors explained an adequate percentage of variance for all SIH items.

SIH-Social Current scale: Three factors had eigenvalues above 1.00 and explained 63% of the variance in the model. The first factor, "Current-Friends," included items 2, 3, and 4, all related to spending time with friends in person, on the phone, or online. The second factor included items 1, 5, and 7 related to spending time with family and going to social events or activities outside the home. Verbal IQ had a negative loading on this "Current-Family/Outside Activities" factor. The last factor was named the "Current-Hobby" factor, because it was driven by Item 6: Doing a hobby at home. The only other item to load on this factor was Age, yet it was judged to be a "real" factor despite its low population because Item 6 had a loading of .81, and the factor explained 15% of the model variance. All factors were correlated below r=.15.

SIH-Social Wishes scale: Three factors had eigenvalues above 1.00 and explained 60% of the variance in the Social Wishes model. The first factor, "Desired-Friends," included the same items as Factor 1 of SIH-SC. The second factor of Social Wishes, however, included items 1 and 6, related to spending time with family and doing a hobby at home. Chronological age and verbal IQ had negative loadings on this "Desired-Family/Hobby" factor. The last SW factor, "Desired-Social Events" was clearly related to social events and activities outside of the house (items 5 and 7). Each factor accounted for 16-25% of the model variance, and all were positively (though not strongly) correlated.

Social Motivation/Participation Disparity as a predictor of depression

SIH factors as predictors of BDI totals and clinical diagnosis

On the assumption that higher social motivation and lower actual participation would be associated with higher BDI scores, interaction terms were calculated for "Current-Friends" by "Desired-Friends" and all other relevant pairs ("Current-Family/Outside Activities" by "Desired-Family/Hobby"; "Current-Family/Outside Activities" by "Desired-Social Events"; and "Current-Hobby" by "Desired-Family/Hobby"). Multiple linear regression models were generated controlling for standardized age and verbal IQ, each of the two independent terms, and the interaction term. For example, one such model might include the following predictors: Age-centered, VIQ-centered, "Current-Friends," "Desired-Friends," "Current-Friends x Desired-Friends Interaction." Verbal IQ was dropped due to consistent non-significant results and parameter constraints. Though age approached significance in some of the models, none of the independent factors or interaction terms predicted BDI scores, contrary to

expectations. Logistic regression was conducted with the same predictors, again with no significant results.

In graphing the (nonsignificant) interaction terms, it appeared that individuals with lower social interest (on any of the SW domains) *and* lower social participation (on the corresponding SC domain) have the highest levels of depressive symptoms on the BDI (see Figure 4.1). Individuals with higher social participation tend to have BDI scores in the "no concern" range, regardless of level of social interest or motivation.

Early "Shared Enjoyment" as a predictor of BDI totals

We postulated that one reason for the findings above is that depression itself affects social motivation. It was possible that, by measuring depressive symptoms and social motivation simultaneously, we were getting Social Wishes responses that had already been negatively affected by depressed mood. No clear pre-depression rating of Social Motivation exists in our data, so we used the "Shared Enjoyment" subtotal on the Autism Diagnostic Interview-Revised (ADI-R) diagnostic algorithm as a stand-in for trait-level Social Motivation. This subtotal indicates parents' retrospective ratings of their children at age 4-5 on the concepts of Showing and Directing Attention, Offering to Share, and Seeking to Share Enjoyment With Others. Higher scores on this total indicate more impairment, i.e., less socially-motivated behavior. This method of using this ADI-R subtotal as a stand-in is limited in that (1) we do not know how stable Shared Enjoyment behaviors would be from ages 4-5 through adulthood, and (2) impairments in Shared Enjoyment might not equate to lack of motivation but rather inherent lack of skill to seek such social input.

The following predictors were entered into a linear regression model predicting BDI scores: standardized chronological age, the SIH "Current-Friends" factor, the ADI-R Shared Enjoyment algorithm subtotal, Age 4-5 (which had been reverse-scored so that increasing scores denote higher social interest, then centered at the sample mean), and the interaction of the Current-Friendship factor and Shared Enjoyment recoded total. Age, Shared Enjoyment at 4-5, and the interaction of current participation with friends and seeking to share enjoyment at 4-5 were all significant terms in the model (see Table 4.7). The direction of the results was again contrary to our expectations for autism: Lower sharing of enjoyment at 4-5 and lower current participation with friends predicted the highest level of depressive symptoms (see Figure 4.2), suggesting that people with less positive social affect earlier in life may have fewer positive interactions and greater levels of depressive symptoms in adolescence and adulthood. The next highest group was those with both higher shared enjoyment at 4-5 and higher current participation with friends.

Discussion

Summary of primary findings

In this study of depressive symptoms in adolescents and adults with autism spectrum disorders, we found evidence to support the high prevalence of depressive features in ASD, with 17% of the sample meeting criteria for a clinical diagnosis of a mood disorder and 51% of the sample scoring in the range of mild clinical concern or above on the Beck Depression Inventory. Of those with clinical diagnoses of depressive disorders, 75% (n=6) scored in the moderate to severe range on the BDI; the remaining 2 individuals scored in the minimal concern range, indicating the need for future study of

the utility of common measures of depression in the ASD population. More encouragingly, BDI scores were only minimally associated with age and were not associated with verbal IQ level in this sample that ranged from mid-adolescence through mid-adulthood and borderline cognitive functioning through above average intelligence. The ability of this instrument to quantify depressive symptoms within the More Able ASD population does not appear to be confounded by these participant characteristics.

Insight into autism-related impairments, as operationalized by proband-rated Behavioral Perception Inventory total scores, predicted higher levels of depressive symptomatology on the Beck Depression Inventory, even when controlling for examiner-rated BPI totals that indicate actual levels of impairment. Insight into *social* impairments, as operationalized by factor scores of differences in examiner- and proband-rated Behavioral Perception Inventory item scores, did not predict higher BDI scores as expected. However, insight into functional independence limitations, measured by scores on this factor of the BPI, was a significant predictor of BDI scores, with greater Examiner-Proband agreement (i.e., proband oversensitivity) associated with higher levels of depressive symptoms. The BPI factor "Insight into Compulsive/Ritualized Behavior" predicted binary clinical diagnosis of depression in the direction that poor insight into these behaviors was associated with the diagnosis of a depressive disorder. Contrary to our hypothesis, unfulfilled social motivation did not predict BDI scores. When both social participation and social motivation were low, greater depressive symptomatology tended to be noted on the BDI. Insight into ASD-associated impairments and social interest and participation, as operationalized by the new measures created for this study, were independent of chronological age and verbal IQ.

Instrumentation

The Behavioral Perception Inventory showed evidence of good internal consistency. Factors derived from Part A of each item, requiring the respondent to rate his/her own behavior, had a more theoretically meaningful factor structure and resulted in significant associations with the outcome measure (BDI scores) compared with Part B items, which asked respondents to rate the degree to which *others* perceive a given behavior in the proband him/herself. Part B items clearly required a higher level of abstract thinking, and were likely too verbally complex for many individuals to rate consistently. The seven people whose data were excluded for highly inconsistent ratings on the BPI 'validity check' items ranged across verbal IQ levels from 72 to 126, however all were 20 years of age or younger. Rating of others' perceptions of one's self may be especially difficult for adolescents in this population. Exploratory factor analysis of the BPI Examiner-Proband difference scores indicated some predictive items and potentially meaningful factors, however this procedure was likely underpowered.

The Social Interests and Habits Questionnaire, created to operationalize Social Motivation and Social Participation, had low Cronbach's alpha coefficients within these subscales. This was likely due to the presence of a strong "Hobby" factor that was negatively correlated with the rest of the social interest factors. This factor was driven largely by one item that assessed interest in doing hobbies at home (which encompasses solitary activity); due to the small number of items assessed in the overall subscales (seven), this item could have significant impact on representations of internal consistency. Factors extracted from the SIH seemed meaningful, but again were based on very few items.

Implications about insight

The predictive significance of the "Functional Independence" factor on BPI scores was robust despite a small sample size and was not explained by direct effects of adaptive behavior impairments themselves. This suggests that *knowing* that one is limited in achieving certain goals or functioning independently at the same level as one's peers is likely a catalyst for depression, in contrast to the *existence* of these limitations alone. Insight into limited realistic goals and independence in caring for one's self could signify an understandable negative response to true limitations. It could also be an artifact of depression itself, in that depressed respondents were more likely to rate themselves as impaired in this way. On the other hand, we might have then expected a halo effect, with the depressive group also endorsing poor social skills and other limitations on the BPI. This association between awareness of symptoms and depressive scores was limited to the Functional Independence factor.

Poor insight into compulsive or ritualized behavior was associated with clinical diagnoses of depression. This also may be an artifact within this small sample, but if replicated in others, requires closer examination. Again, contrary to expectations, insight into social impairments did not predict depressive symptoms or disorders. This also necessitates follow-up studies in independent samples to explore whether the finding is driven by measurement inaccuracy, or whether there is a need to revisit the assumption that higher cognitive abilities are associated with more depression due to higher levels of insight into social limitations caused by ASD.

Implications about social motivation and participation

Differences in factor structure across the Social Wishes and Social Current subscales indicate that there is a mismatch between desired and actual social participation in adolescents and adults with ASD. Desire to spend time with one's family or doing a hobby at home loaded together, while desire for outside events and activities loaded on a separate factor. Current opportunities to socialize loaded separately onto a Family/Outside Events factor and onto a Hobby factor. This suggests that adolescents' and adults' participation in activities outside the home are associated with, and likely mediated by, time spent with their families, though they may wish to participate in outside events and activities independently. If replicated in a larger sample, further exploration of these patterns may help in making recommendations for families in terms of facilitating social participation for adolescents and adults with ASD.

In terms of the hypothesis that discrepancy between social motivation and participation would predict depressive features, the group we predicted would have highest depression totals actually had among the lowest in our sample. That is, individuals with higher social motivation and lower social participation did not appear to be particularly affected by depressive symptomatology. The group that tended toward the highest BDI scores showed a profile of low social motivation and low social participation. For some participants at least, depression may be the causal factor of this profile instead of the reverse, and thus our hypothesis could not be measured fully due to the absence of social motivation data that pre-dated onset (or increase) of depressive symptoms. However, these results do underscore the urgent need to study treatment for depression in ASD, as this comorbid disorder may exacerbate problems with motivation

to participate in the social world – when such participation is already compromised within the autism spectrum.

Attempts were made to use the "Shared Enjoyment" algorithm subtotal of the ADI-R as a trait-level measure of Social Motivation unbiased by current depression. This was limited in that these scores rated proband social initiations at age 4-5, usually through retrospective parent report; it is unclear whether seeking to share enjoyment and make other social initiations at age 4-5 generally would stay stable through adulthood within this population. This hypothesis would be better explored with a trait-based measure of Social Motivation that focuses on the concept prior to onset of depressive features.

Implications for treatment

The findings from this study, though preliminary, have important implications for treatment of depressive disorders in ASD. Adaptive behavior appears to influence and be influenced by depression. The awareness of deficits in functional independence, rather than social skill, were associated with symptoms of depression in this sample. This would suggest that, in order to ameliorate depressive symptoms in people with More Able ASD, it is important to work to improve adaptive competence and independent living skills. Because the *awareness* of these limitations appears to be significant, psychoeducation about ASD, intended to build understanding of one's own real impairments and to explore strengths, as well as cognitive behavioral strategies promoting tolerance of negative affect and undesired realities, also may be beneficial in depression prevention and intervention in this population.

We had limited capability to test unfulfilled social motivation and participation as predictors of depressive symptoms because of the potential effects of depression on the "independent" variables. However, findings from this study, though preliminary, suggest that more direct treatment to promote social motivation (e.g., identifying and providing motivators for social behavior) and to improve adaptive skills is needed in the More Able ASD population.

Limitations

The findings are limited by small sample size and measures that require validation. The sample size, which varied from 33 to 46 by analysis, due to missing or invalid data, led to underpowered analyses in this study, particularly with regard to BPI exploratory factor analysis and regression models. A number of other important predictors (such as rumination and perceived social support) could not be included in multinomial regression models in order to accommodate the control variables and predictors of interest. Smaller sample size results in larger standard errors for regression coefficients and thus limits power to detect relationships. On the other hand, BPI Functional Independence (Part A, Factor 3) had consistently significant effects despite these limitations.

Recruitment bias may exist in this sample. The community recruitment strategies and consent form information were explicit regarding this as a study of "well-being" and "emotional health," which potentially could have attracted more people with emotional health concerns.

Interrater and test-retest reliability have not yet been established for the newly created study measures, the BPI and SIH. The BPI "Functional Independence" factor was

strong in terms of factor loadings and model variance explained, but nonetheless was based largely on two items of untested validity to measure insight into adaptive behavior. The present data may be useful as pilot data in expanding the examples to make a stronger measure of insight into functional impairments common to the autism spectrum.

Future Directions

Validation studies in ASD samples are needed for depression measures with strong predictive performance in the general population. We have much to learn about presentation of depression in ASD through (1) descriptions of items endorsed most and least frequently in the ASD population, (2) comparison of self- and parent-report instruments, and (3) examination of various measures' (including the BDI's) agreement with clinical diagnosis of depressive disorders. The role of different age groups in the trajectory of depression in ASD should also be explored, as well as similarities in presentation and prevalence of depression in other developmental disabilities to explore the specificity to ASD of comorbid depression. As a field, we also need to develop the means to assess and treat mood disorders in individuals with limited language and intellectual disabilities. Because of the specific recruitment of individuals with borderline to above average intelligence for this sample, these findings cannot be generalized to the broader population of individuals with ASD; different paths and predictors of depression likely exist for less able ASD populations.

Exploration of psychosocial mechanisms underlying depressive symptoms in More Able ASD should inform treatment development, for example whether comprehensive treatment designed to modify multiple functioning domains is indicated as a means to enhance motivation and quality of life in this population beyond "treatment

as usual" for depression. We plan to explore other risk and protective factors to depressive symptoms in this population, such as rumination, repetitive behaviors, perceived social support, and reciprocity of friendship. Ultimately, we hope that providing relatively inexpensive treatments of co-occurring problems in ASD in a timely manner will prove effective in changing the quality of life of adults with ASD and their families.

Table 4.1 Recruitment and Participation Description

	Michigan Pool (n=52)	**Longitudinal Pool (n=53)**	**Overall Pool (n=105)**
Participated; Data used	25 (48%)	21 (40%)	46 (44%)
Participated but Ineligible	2 (4%)	24 (45%)	26 (25%)
No Response /Not scheduled in Time	14 (27%)	8 (15%)	33 (31%)
Declined	11 (21%)		

Table 4.2 Sample Description

	N	Range	Mean(SD)
Age in Years	46	15-31	21 (4.2)
VIQ	46	72-140	106.2 (17.4)
NVIQ	46	74-138	103.9 (15.7)
ADI-R Social	45	2-30	16.0 (8.0)
ADI-R CommV	45	0-24	13.2 (6.3)
ADI-R CommNV	45	0-14	7.4 (4.4)
ADI-R RRB	46	0-12	6.0 (3.1)
ADOS SA	9	2-12	6.9 (2.8)
ADOS RRB	9	0-6	3.4 (2.0)
ADOS Comm	43	0-5	2.7 (1.4)
ADOS Soc	43	0-14	6.5 (2.9)
ADOS Comm-Soc	43	0-18	9.2 (3.9)
ADOS Stereo	43	0-6	1.1 (1.5)
VCST	45	33-113	74.9 (18.2)
VDLST	46	36-109	72.9 (14.4)
VSST	46	25-119	71.7 (17.1)
VABCST	45	28-119	70.1 (15.0)
BDI	45	0-28	10.6 (7.9)
SRDQ	46	38-71	51.8 (9.2)
CDRS	30	14-62	28.0 (10.8)
CDI-Parent	24	2-27	16.5 (6.4)

Note. VIQ=Verbal IQ; NVIQ=Nonverbal IQ; ADI-R Social=ADI-R Social Total; ADI-R CommV=ADI-R Communication Total for Verbal Subjects; ADI-R CommNV=ADI-R Communication Total for Nonverbal Subjects; ADI-R RRB=ADI-R Restricted, Repetitive Behaviors Total; ADOS SA=ADOS Social Affect Total (Module 3); ADOS RRB=ADOS Restricted Repetitive Behavior Total (Module 3); ADOS Comm=ADOS Communication Total (Module 4); ADOS Soc=ADOS Reciprocal Social Interaction Total (Module 4); ADOS Comm-Soc=ADOS Communication+Reciprocal Social Combined Total (Module 4); ADOS Stereo=ADOS Stereotyped Behavior and Restricted Interests Total (Module 4); VCST=Vineland II Communication standard score; VDLST=Vineland II Daily Living Skills standard score; VSST=Vineland II Socialization standard score; VABCST=Vineland II Overall Adaptive Behavior Composite standard score; BDI=Beck Depression Inventory-II total; SRDQ=Self-Report Depression Questionnaire total; CDRS=Children's Depression Rating Scale total score (adapted for adults); CDI-Parent=Children's Depression Inventory, Parent Version, total score (adapted for adults).

Table 4.3 Parent Participant Description

Reporter/ *Marital Status*	**Mother**	**Father**	**Both**	***Married***	***Single Mother***	***Single Father***
Michigan Recruits (n=25)	19 (76%)	5 (20%)	1 (4%)	16 (64%)	7 (28%)	2 (8%)
Longitudinal Recruits (n=21)	19 (90%)	1 (5%)	1 (5%)	12 (57%)	8 (38%)	1 (5%)
Overall Sample (n=46)	38 (83%)	6 (13%)	2 (4%)	28 (61%)	15 (33%)	3 (6%)

Table 4.4 Measure Protocol

Adolescent		Dependent Adult		Independent Adult	
Proband	Parent	Proband	Parent	Proband	Parent
MAILED PACKET	MAILED PACKET	MAILED PACKET	MAILED PACKET	MAILED PACKET	MAILED PACKET
Spence Children's Anxiety Scale (SCAS)[3]	Spence Children's Anxiety Scale-Parent Report (SCAS-PR)[3]	Adult Manifest Anxiety Scale (AMAS)[3]	Spence Children's Anxiety Scale-Parent Report – ADAPTED (SCAS-PR)[3]	Adult Manifest Anxiety Scale (AMAS)[3]	Spence Children's Anxiety Scale-Parent Report – ADAPTED (SCAS-PR)[3]
Youth Self Report (YSR)[4]	Child Behavior Checklist (CBCL)[4]	Adult Self Report (ASR)[4]	Adult Behavior Checklist (ABCL)[7]	Adult Self Report (ASR)[4]	Adult Behavior Checklist (ABCL)[7]
Ruminative Response Scale (RRS)[9]		Ruminative Response Scale (RRS)[9]		Ruminative Response Scale (RRS)[9]	
Asher Loneliness Scale[9]		Asher Loneliness Scale[9]		Asher Loneliness Scale[9]	
Life Orientation Scale (LOT-R)[10]		Life Orientation Scale (LOT-R)[10]		Life Orientation Scale (LOT-R)[10]	
Autism Spectrum Quotient (AQ)[11]		Autism Spectrum Quotient (AQ)[11]		Autism Spectrum Quotient (AQ)[11]	
ASSESSMENT	ASSESSMENT	ASSESSMENT	ASSESSMENT	ASSESSMENT	ASSESSMENT
Wechsler Abbreviated Intelligence Scale (WASI)[12]	Autism Diagnostic Interview-Revised (ADI-R)[13]	Wechsler Abbreviated Intelligence Scale (WASI)[12]	Autism Diagnostic Interview-Revised (ADI-R)[13]	Wechsler Abbreviated Intelligence Scale (WASI)[12]	Autism Diagnostic Interview-Revised (ADI-R)[13]
Self-Report Depression Questionnaire[14]	Family History of Mental Health	Self-Report Depression Questionnaire[14]	Family History of Mental Health	Self-Report Depression Questionnaire[14]	Family History of Mental Health
Autism Diagnostic Observation Schedule[15]	Vineland Adaptive Behavior Scales (Vineland II)[16]	Autism Diagnostic Observation Schedule[15]	Vineland Adaptive Behavior Scales (Vineland II)[16]	Autism Diagnostic Observation Schedule[15]	Vineland Adaptive Behavior Scales (Vineland II)[16]
Behavioral Perception Inventory (BPI-Pr)[17]	Behavioral Perception Inventory (BPI-P/C)[17]	Behavioral Perception Inventory (BPI-P)[17]	Behavioral Perception Inventory (BPI-P/C)[17]	Behavioral Perception Inventory (BPI-P)[17]	Behavioral Perception Inventory (BPI-P/C)[17]
Social Interests and Habits Questionnaire (SIH)[18]	Children's Depression Rating Scale (CDRS), ADAPTED[19]	Social Interests and Habits Questionnaire (SIH)[18]	Children's Depression Rating Scale (CDRS), ADAPTED[19]	Social Interests and Habits Questionnaire (SIH)[18]	Children's Depression Rating Scale (CDRS), ADAPTED[19]
Beck Depression Inventory (BDI-II)[20] OR Children's Depression Inventory (CDI)[21]	Children's Depression Inventory-Parent Report (CDI-P)[22]	Beck Depression Inventory (BDI-II)[20]	Children's Depression Inventory-Parent Report (CDI-P)[22]	Beck Depression Inventory (BDI-II)[20]	Children's Depression Inventory-Parent Report (CDI-P)[22]
Sarason Social Support Q (SSQ)[23]		Sarason Social Support Q (SSQ)[23]		Sarason Social Support Q (SSQ)[23]	
Neale Analysis of Reading (NARA)[24] OR Wide Range Achievement Test (WRAT)[25]		Neale Analysis of Reading (NARA)[24] OR Wide Range Achievement Test (WRAT)[25]		Neale Analysis of Reading (NARA)[24] OR Wide Range Achievement Test (WRAT)[25]	

[1]Spence, Barrett, & Turner, 2003
[2]Nauta et al., 2004
[3]Lowe & Reynolds, 2004
[4]Achenbach, 1991
[5]Achenbach & Rescorla, 2000
[6]Achenbach, 1997
[7]Tenneij & Koot, 2007
[8]Nolen-Hoeksema & Jackson, 2001
[9]Asher, Hymel, & Renshaw, 1984
[10]Scheier, Carver, & Bridges, 1994
[11]Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001
[12]Wechsler, 1999
[13]Rutter, LeCouteur, & Lord, 2003
[14]Reynolds & Baker, 1988
[15]Lord et al., 2000
[16]Sparrow, Cicchetti, & Balla, 2005
[17]Gotham, Bishop, & Lord, unpublished
[18]Bishop, Gotham, & Lord, unpublished
[19]Poznanski & Mokros, 1996
[20]Beck, 1996
[21]Kovacs, 1992
[22]Wierzbicki, 1987
[23]Sarason, Sarason, Shearling, & Pierce, 1987
[24]Neale, 1997
[25]Wilkinson & Robertson, 2006

Table 4.5 Factor Loadings from Behavioral Perception Inventory Examiner-Proband Difference scores

		Ex-Prb (Self)			Ex-Prb (Others)			
Item Number	BPI Item Description	Fctr 1	Fctr 2	Fctr 3	Fctr 1	Fctr 2	Fctr 3	Fctr 4
2	Comfort-routine		.79		.86			
3	Notices details		.60		.54			
4	Make friends I	.65					.72	
5	Forgets to ask I	.59			.72			
6	Realistic goals			.76				.76
7	Rude/inappropriate	.42			.66			
9	Specific order		.41		.36			
10	Senses boredom	.54			.42			
11	Comfort-social	.58			--	--	--	--
12	Interrupts	.54			.62			
13	Hyper-focus	.59			.35			
14	Stands too close		-.49			.65		
15	Conversation I	.71				.59		
16	Talks about 1 thing	.62			.40			
17	Hand mannerisms	.49			--	--	--	--
19	Make friends II	.69					.66	
20	Independent			.71		.66		
21	Monopolizes talk	.65			.60			
22	Unusual words	.45			.56			
23	Upset-routine change		.64		.79			
24	Forgets to ask II	.44			.68			
25	Gets sarcasm	.43					.69	
26	Conversation II	.64				.53		
28	Eye contact			-.46				-.62
29	Control anger/anx	--	--	--				.51
30	Doesn't stop talking	.83			.48			
32	Reads facial expressions	.37					.70	
33	Pays attention	.64				.84		
	Age	--	--	--		-.64		
	VIQ	--	--	--		-.49		
Eigenvalue		7.3	3.1	2.3	6.3	3.4	2.5	2.0
% Var Explained		24.4	10.4	7.6	20.9	11.3	8.5	6.8

Note. Ex-Prb(Self)=Behavioral Perception Inventory Difference Scores for Examiner – Proband Part A (Proband rating own behavior). Ex-Prb(Others)= Behavioral Perception Inventory Difference Scores for Examiner – Proband Part B (Proband rating others'perception of proband's behavior).

Note. Items with factor loadings less than the absolute value of .35 are denoted with "--."

Table 4.6 Multiple Linear Regression Model: Standardized Age and Behavioral Perception Inventory (Part A) Factor Scores Predicting Beck Depression Inventory Total Scores

DV=BDI Total Scores (N=36)						
	R^2	**F change**	**df**	**B**	**SE B**	**β**
Constant**	.30	3.13	4,30	10.64	1.3	
Age (Zscore)				2.38	1.2	.31
Insight-Convs				-1.46	1.3	-.17
Insight-Comp/Rit				.07	1.3	.01
Insight-Func Ind*				-3.51	1.3	-.43

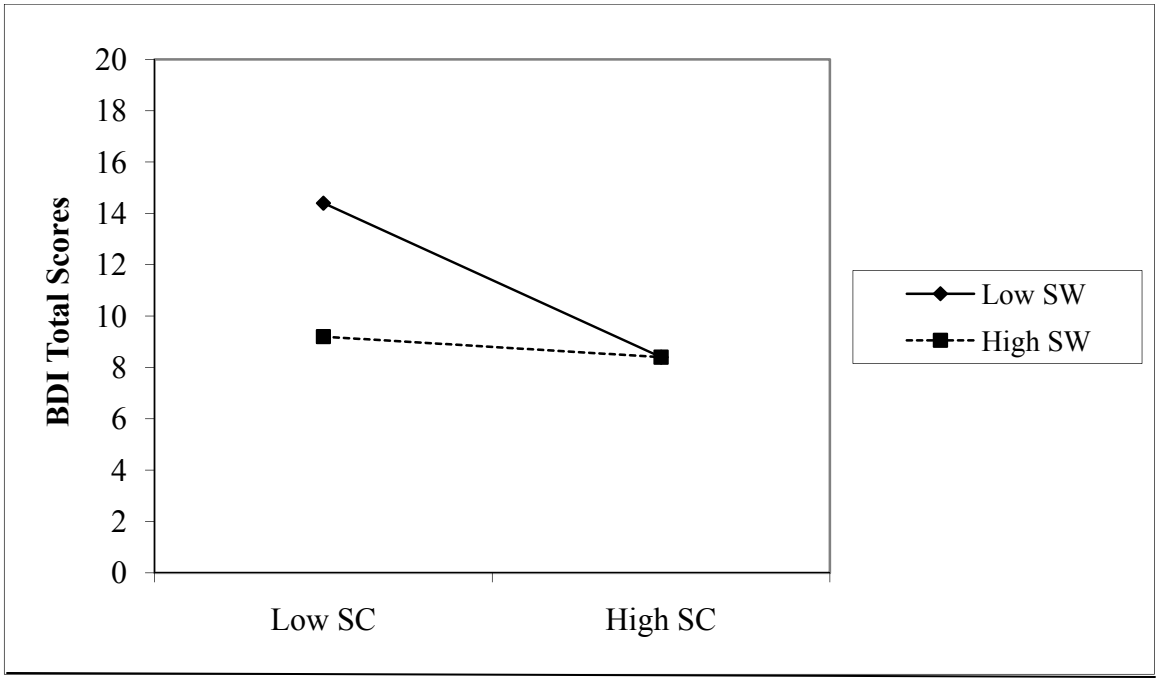
Note. DV=Dependent variable; Age (Zscore)=Chronological Age as Z-scores; Insight-Convs=Factor 1 of BPI Part A, 3-factor solution, "Insight into Conversation/ Monologue"; Insight-Comp/Rit=Factor 2 of BPI Part A, 3-factor solution, "Insight into Compulsive/Ritualized"; Insight-Func Ind=Factor 3 of BPI Part A, 3-factor solution, "Insight into Functional Independence."
* p<.01, ** p<.001

Table 4.7 Multiple Linear Regression Model: Social Motivation and Participation Measures as Predictors of Beck Depression Inventory Total Scores

	DV=BDI Total Scores (N=43)					
	R^2	**F change**	**df**	**B**	**SE B**	**β**
Constant**	.48	8.82	4,39	9.84	.93	
Age (Zscore)*				3.53	.97	.44
Current-Friend				-.38	.96	-.05
Shrnj 4-5 (Zscore)*				-2.62	.96	-.32
Shrnj x Current-Friend**				4.41	1.01	.55

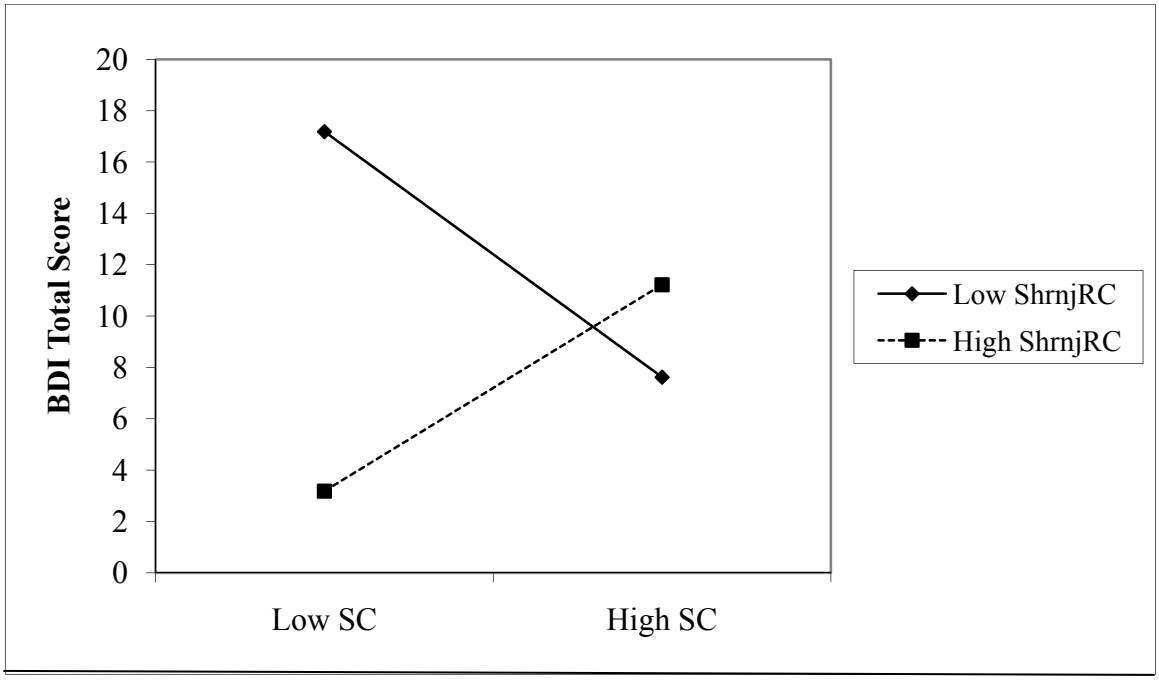
Note. DV=Dependent variable; Age (Zscore)=Chronological Age as Z-scores; Current-Friend=Social Interests and Habits Questionnaire-Social Current Factor 1, "Current-Friend"; Shrnj4-5(Zscore)=Autism Diagnostic Interview-Revised "Shared Enjoyment" algorithm subtotal from Age 4-5 retrospective Report, standardized; ShrnjxCurrent-Friend=Interaction term between SIH-SC Factor 1 and ADI-R Shared Enjoyment subtotal Z scores.
* $p<.01$, ** $p<.001$

Figure 4.1 Interaction of Social Interests and Habits Questionnaire Friendship Factors—Social Current by Social Wishes



Note. Low SC=Lower current social participation with friends as measured by factor scores on the Social Interests and Habits Questionnaire (SIH), Social Current subscale.
High SC=Higher current social participation with friends as measured by factor scores on the SIH, Social Current subscale.
Low SW=Lower desired social participation ("social motivation") with friends as measured by factor scores on the SIH, Social Wishes subscale.
High SW=Higher desired social participation ("social motivation") with friends as measured by factor scores on the SIH, Social Wishes subscale.

Figure 4.2 Interaction of Social Interests and Habits Questionnaire "Current-Friendship" Factor by Autism Diagnostic Interview-Revised "Shared Enjoyment" Algorithm Total, Age 4-5, Recoded



Note. Low SC=Lower current social participation with friends as measured by factor scores on the Social Interests and Habits Questionnaire (SIH), Social Current subscale.
High SC=Higher current social participation with friends as measured by factor scores on the SIH, Social Current subscale.
Low ShrnjRC=Less evidence of social motivation as measured by the Shared Enjoyment algorithm subscale of the Autism Diagnostic Interview-Revised (ADI-R), age 4-5 report.
High ShrnjRC=More evidence of social motivation as measured by the Shared Enjoyment algorithm subscale of the Autism Diagnostic Interview-Revised (ADI-R), age 4-5 report.

Appendix A: Behavioral Perception Inventory

List of Measures

For Box A:

Circle <u>what you think about yourself.</u>

EXAMPLE

A.

Do you tell funny jokes?			
Almost Never	A Little	Pretty Much	Almost Always

For Box B:

Circle what <u>other people think about you</u>.

EXAMPLE

B.

How much do other people think you tell funny jokes?			
Not Much	A Little	Pretty Much	Very Much

Who thinks that about you? How can you tell?

1.

A.

Are you an honest person?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* are an honest person?			
Not Much	A Little	Pretty Much	Very Much

2.

A.

Do you feel more comfortable when things happen the same way every time?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* feel more comfortable when things happen the same way every time?			
Not Much	A Little	Pretty Much	Very Much

3.

A.

Do you notice or remember details that most people do not?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* notice or remember details that most people do not?			
Not Much	A Little	Pretty Much	Very Much

4.

A.

Is it easy for you to make new friends?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think* that it is easy for *you* to make new friends?			
Not Much	A Little	Pretty Much	Very Much

5.

A.

Do you forget to ask people about their interests or experiences?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* forget to ask people about their interests or experiences?			
Not Much	A Little	Pretty Much	Very Much

6.

A.

Are your dreams and goals for the future realistic?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think your* dreams and goals for the future are realistic?			
Not Much	A Little	Pretty Much	Very Much

7.

A.

Do you do things that are rude or inappropriate even when you don't mean to?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* do things that are rude or inappropriate?			
Not Much	A Little	Pretty Much	Very Much

8.

A.

Do you spend time doing things you enjoy (like reading or watching TV)?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* spend time doing things you enjoy?			
Not Much	A Little	Pretty Much	Very Much

9.

A.

Do you like certain things to be placed in a very specific way, or happen in a very specific order?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* like certain things to be in a specific placement or order?			
Not Much	A Little	Pretty Much	Very Much

10.

A.

Can you tell when someone is getting bored listening to you?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* can tell when someone is getting bored listening to you?			
Not Much	A Little	Pretty Much	Very Much

11.

A.

Do you feel comfortable in social situations?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* feel comfortable in social situations?			
Not Much	A Little	Pretty Much	Very Much

12.

A.

Do you interrupt people when they are talking?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* interrupt people when they are talking?			
Not Much	A Little	Pretty Much	Very Much

13.

A.

Do you get so involved in doing some things that you forget about other things?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* get so involved in doing some things that you forget about other things?			
Not Much	A Little	Pretty Much	Very Much

14.

A.

Do you stand too close to people?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* stand too close to people?			
Not Much	A Little	Pretty Much	Very Much

15.

A.

Is it easy for you to keep a conversation going?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think* it is easy for *you* to keep a conversation going?			
Not Much	A Little	Pretty Much	Very Much

16.

A.

Do you spend too much time talking about your favorite things?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* spend too much time talking about your favorite things?			
Not Much	A Little	Pretty Much	Very Much

17.

A.

Do you move your hands or fingers in unusual ways, like flapping or twisting them?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* move your hands or fingers in unusual ways?			
Not Much	A Little	Pretty Much	Very Much

18.

A.

Are you a kind and caring person?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* are a kind and caring person?			
Not Much	A Little	Pretty Much	Very Much

19.

A.

Is it difficult for you to make new friends?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think* that it is difficult for *you* to make new friends?			
Not Much	A Little	Pretty Much	Very Much

20.

A.

Are you independent in taking care of yourself?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* are independent in taking care of yourself?			
Not Much	A Little	Pretty Much	Very Much

21.

A.

Do you forget to give people a turn to talk when you are excited about a conversation topic?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* forget to give people a turn to talk when you are excited about a topic?			
Not Much	A Little	Pretty Much	Very Much

22.

A.

Do you use words or expressions that other people do not use as much?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* use words or expressions that other people do not use as much?			
Not Much	A Little	Pretty Much	Very Much

23.

A.

Do you get upset when your daily routine is disturbed?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* get upset when your daily routine is disturbed?			
Not Much	A Little	Pretty Much	Very Much

24.

A.

Do you remember to ask people about their experiences or interests?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* ask people about their experiences or interests?			
Not Much	A Little	Pretty Much	Very Much

25.

A.

Can you tell when someone is kidding or being sarcastic?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* can tell when someone is kidding or being sarcastic?			
Not Much	A Little	Pretty Much	Very Much

26.

A.

Is it difficult for you to keep a conversation going?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think* it is difficult for *you* to keep a conversation going?			
Not Much	A Little	Pretty Much	Very Much

27.

A.

Do you keep yourself clean and dressed appropriately?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* keep yourself clean and dressed appropriately?			
Not Much	A Little	Pretty Much	Very Much

28.

A.

Do you look people in the eyes when talking to or doing things with them?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* look people in the eyes when talking to or doing things with them?			
Not Much	A Little	Pretty Much	Very Much

29.

A.

Can you control your anger and anxiety?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* can control your anger and anxiety?			
Not Much	A Little	Pretty Much	Very Much

30.

A.

Do you have trouble knowing when to stop talking?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* have trouble knowing when to stop talking?			
Not Much	A Little	Pretty Much	Very Much

31.

A.

Do you take care of your own money and finances?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* take care of your own money and finances?			
Not Much	A Little	Pretty Much	Very Much

32.

A.

Can you figure out how someone feels just by looking at his or her face?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* can figure out how someone feels just by looking at his/her face?			
Not Much	A Little	Pretty Much	Very Much

33.

A.

Is it difficult for you to keep your attention where it is supposed to be?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think* it is difficult for *you* to keep your attention where it is supposed to be?			
Not Much	A Little	Pretty Much	Very Much

34.

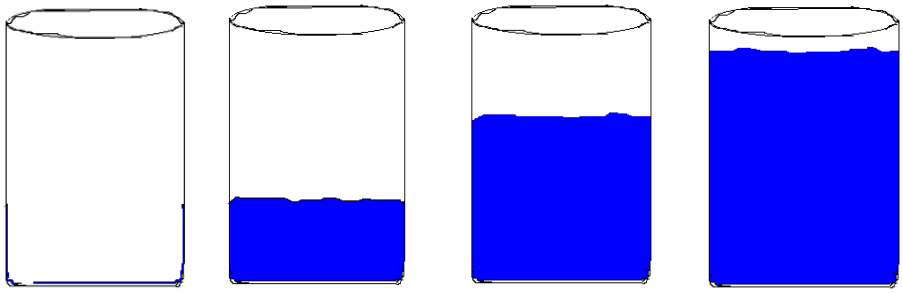
A.

Do you have hopes and dreams for the future?			
Almost Never	A Little	Pretty Much	Almost Always

B.

How much do *others think you* have hopes and dreams for the future?			
Not Much	A Little	Pretty Much	Very Much

BPI Response Options



Almost Never

or

Not Much

A Little

Pretty Much

Almost Always

or

Very Much

BEHAVIORAL PERCEPTION INVENTORY (BPI): Parent/Caregiver

This form filled out about (name): _____Date of Birth:_____

This form filled out by (name):_____Relationship: _____

Today's Date._____

How to fill out the questionnaire

Please read each statement very carefully and rate how much that describes your child by circling your answer from the options listed below the question.

Example:

1. _____ tells funny jokes.				← Does ___ think that is true about him/herself?		
(Almost Never)	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

Then, move over to the right-hand side of the box, and think about whether your child thinks that statement is true about him/herself. Circle "Yes" or "No."

1. _____ tells funny jokes.				← Does ___ think that is true about him/herself?		
(Almost Never)	A Little	Pretty Much	Almost Always	NO	(YES)	Not Sure

In the example above, you feel that your child does not often tell funny jokes (circled ALMOST NEVER), but you feel that your child thinks he/she does tell funny jokes (circled YES).

Please respond about your child:

1. _____ is honest.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

2. _____ feels more comfortable when things happen the same way every time.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

3. _____ notices or remembers details that others do not.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

4. _____ finds it easy to make new friends.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

5. _____ forgets to ask other people about their interests or experiences.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

6. When _____ sets long-term goals, they are realistic.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

7. _____ does things that seem rude or inappropriate when he/she doesn't mean for them to be.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

Please respond about your child:

8. _____ spends time doing things he/she enjoys (like reading or watching TV).				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

9. _____ likes certain things to be placed in a very specific way, or happen in a very specific order.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

10. _____can tell when someone is getting bored while listening to him/her.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

11. _____ is comfortable in social situations.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

12. _____ interrupts others when they're talking.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

13. _____ gets wrapped up in things he/she is doing and loses sight of other things.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

14. _____ stands too close to people.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

Please respond about your child:

15. It is easy for _____ to keep a conversation going.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

16. _____ spends too much time talking about his/her favorite things.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

17. _____ moves his/her hands or fingers in ways that not many other people do, like flapping or twisting them.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

18. _____ is kind and caring.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

19. It's hard for _____ to make new friends.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

20. _____ is independent in caring for him/herself.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

21. When _____ gets excited about a topic, he/she forgets to give others a turn to talk.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

Please respond about your child:

22. _____ uses words or expressions that other people don't use as much.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

23. _____ feels upset when his/her daily routine is disturbed.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

24. _____ remembers to ask other people about their interests or experiences.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

25. It's hard for _____ to tell when someone is kidding or being sarcastic.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

26. It is difficult for _____ to keep a conversation going.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

27. _____ keeps him/herself clean and dressed appropriately.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

28. _____ does not look people in the eyes as much as other people do.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

Please respond about your child:

29. _____ can control his/her anger and anxiety.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

30. _____ has trouble knowing when to stop talking.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

31. _____ manages his/her own money and financial obligations.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

32. It is easy for _____ to figure out how someone feels just by looking at the person's face.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

33. It is difficult for _____ to keep his/her attention where it's supposed to be.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

34. _____ has goals and dreams for the future.				← Does ___ think that is true about him/herself?		
Almost Never	A Little	Pretty Much	Almost Always	NO	YES	Not Sure

Thank you for your thoughtful responses.

BEHAVIORAL PERCEPTION INVENTORY (BPI): Examiner Form

This form filled out about (name): _____Date of birth:_____

This form filled out by (name):_____

Did you complete the Autism Diagnostic Observation Schedule (ADOS) on the above-named person?

Circle: YES NO

If NO, in what ways did you interact with this person?

_____

_____

Today's Date._____

How to fill out the questionnaire

Please read each statement very carefully and rate how much that describes this participant by circling your answer from the options listed below the question, or circle the "Not applicable" option.

Base your responses on *all* available information from your own experiences with the individual (e.g., ADOS administration, cognitive testing, casual conversation, therapy settings).

Example:

1. _____ likes to exercise.				
Almost Never	A Little	Pretty Much	Almost Always	Not applicable given the information obtained

1. _____ is honest.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

2. _____ feels more comfortable when things happen the same way every time.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

3. _____ notices or remembers details that others do not.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

4. _____ finds it easy to make new friends.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

5. _____ forgets to ask other people about their interests or experiences.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

6. When _____ sets long-term goals, they are realistic.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

7. _____ does things that seem rude or inappropriate when he/she apparently doesn't mean for them to be.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

8. _____ spends time doing things he/she enjoys (like reading or watching TV).				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

9. _____ likes certain things to be placed in a very specific way, or happen in a very specific order.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

10. _____can tell when someone is getting bored while listening to him/her.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

11. _____ is comfortable in social situations.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

12. _____ interrupts others when they're talking.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

13. _____ gets wrapped up in things he/she is doing and loses sight of other things.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

14. _____ stands too close to people.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

15. It is easy for _____ to keep a conversation going.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

16. _____ spends too much time talking about his/her favorite things.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

17. _____ moves his/her hands or fingers in ways that not many other people do, like flapping or twisting them.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

18. _____ is kind and caring.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

19. It's hard for _____ to make new friends.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

20. _____ is independent in caring for him/herself.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

21. When _____ gets excited about a topic, he/she forgets to give others a turn to talk.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

22. _____ uses words or expressions that other people don't use as much.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

23. _____ feels upset when his/her daily routine is disturbed.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

24. _____ remembers to ask other people about their interests or experiences.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

25. It's hard for _____ to tell when someone is kidding or being sarcastic.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

26. It is difficult for _____ to keep a conversation going.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

27. _____ keeps him/herself clean and dressed appropriately.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

28. _____ does not look people in the eyes as much as other people do.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

29. _____ can control his/her anger and anxiety.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

30. _____ has trouble knowing when to stop talking.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

31. _____ manages his/her own money and financial obligations.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

32. It is easy for _____ to figure out how someone feels just by looking at the person's face.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

33. It is difficult for _____ to keep his/her attention where it's supposed to be.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

34. _____ has goals and dreams for the future.				Not applicable given the information obtained
Almost Never	A Little	Pretty Much	Almost Always	

Thank you for your thoughtful responses.

Appendix B: Social Interests and Habits Questionnaire

List of Measures

Social Interests and Habits Questionnaire (SIH-Q)

We want to ask you some questions about **you** and the kinds of things you do. There are no right or wrong answers.

Thinking about you:

1. How often do **you** spend time with family members?

None	A Little	Pretty Much	A Lot

2. How often do **you** spend time with friends?

None	A Little	Pretty Much	A Lot

3. How often do **you** talk on the phone with friends?

None	A Little	Pretty Much	A Lot

4. How often do **you** email or chat online with friends?

None	A Little	Pretty Much	A Lot

5. How often do **you** go to social events (example: social groups, birthday parties, dances, church socials)?

None	A Little	Pretty Much	A Lot

6. How often do **you** do a hobby at home (example: reading a book, playing videogames, doing a puzzle)?

None	A Little	Pretty Much	A Lot

7. How often do **you** do an activity out of the house (example: going bowling, going to a movie, going shopping, going to religious services)?

None	A Little	Pretty Much	A Lot

8. Do you currently have a girlfriend/boyfriend or husband/wife?

YES NO

9. Who are your best friends right now?

_____

_____

_____

_____

_____

10. Do you currently have a job?

YES NO

11. If you do have a job now, where do you work?

_____

12. If you do have a job now, what do you do at your job?

_____

_____

13. What are your favorite things to do?

_____

_____

_____

Name: _____ Date: _____ SW page 1

Social Interests and Habits Questionnaire (SIH-Q)

We want to know how you would spend your time **if you could have your wish**. There are no right or wrong answers.

If you could have your wish:

1. How often would you **want** to spend time with family members?

None	A Little	Pretty Much	A Lot

2. How often would you **want** to spend time with friends?

None	A Little	Pretty Much	A Lot

3. How often would you **want** to talk on the phone with friends?

None	A Little	Pretty Much	A Lot

4. How often would you **want** to email or chat online with friends?

None	A Little	Pretty Much	A Lot

5. How often would you **want** to go to social events (example: social groups, birthday parties, dances, church socials)?

None	A Little	Pretty Much	A Lot

6. How often would you **want** to do a hobby at home (example: reading a book, playing videogames, doing a puzzle)?

None	A Little	Pretty Much	A Lot

7. How often would you **want** to do an activity out of the house (example: going bowling, going to a movie, going shopping, going to religious services)?

None	A Little	Pretty Much	A Lot

If you could have your wish:

8. Would you **want** to have a job someday?

Circle what you would choose:

No	A Little	Pretty Much	A Lot

I have a job now

9. If you got a first job or a new job someday, what kind of job would you **want**?

_____

10. Would you **want** to have a girlfriend/boyfriend someday?

Circle what you would choose:

No	A Little	Pretty Much	A Lot

I have a girlfriend/ boyfriend now

11. Would you **want** to get married someday?

Circle what you would choose:

No	A Little	Pretty Much	A Lot

I am married now

12. Would you **want** to have children someday?

Circle what you would choose:

No	A Little	Pretty Much	A Lot

I have children now

13. How many friends would you **want**? _____

14. What kind of friends would you **want**? _____

15. Are there other things that you wish for? _____

Social Interests and Habits Questionnaire (SIH-Q)

Now we want to ask you some questions about **other people your age** and the kinds of things that they do. There are no right or wrong answers.

Thinking about other people your age:

1. How often do **other people your age** spend time with family members?

None	A Little	Pretty Much	A Lot

2. How often do **other people your age** spend time with friends?

None	A Little	Pretty Much	A Lot

3. How often do **other people your age** talk on the phone with friends?

None	A Little	Pretty Much	A Lot

4. How often do **other people your age** email or chat online with friends?

None	A Little	Pretty Much	A Lot

5. How often do **other people your age** go to social events (example: social groups, birthday parties, dances, church socials)?

None	A Little	Pretty Much	A Lot

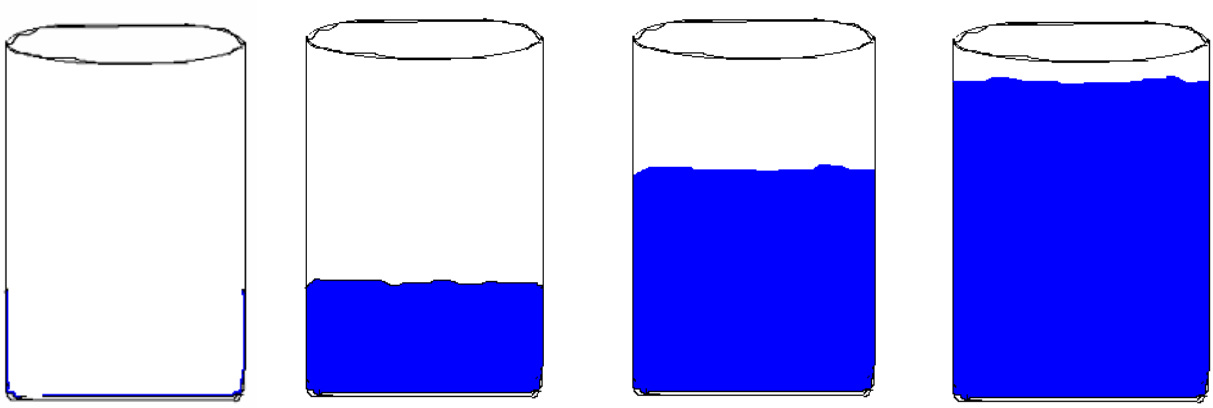
6. How often do **other people your age** do a hobby at home (example: reading a book, playing videogames, doing a puzzle)?

None	A Little	Pretty Much	A Lot

7. How often do **other people your age** do an activity out of the house (example: going bowling, going to a movie, going shopping, going to religious services)?

None	A Little	Pretty Much	A Lot

SIH-Q Response Options



None

<u>or</u>

No

A Little

Pretty Much

A Lot

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Chapter V

Conclusion

Over the last twenty years, improvements in the assessment of autism spectrum disorders (ASD) have been associated with greater comparability of findings across research projects and the ability to reliably describe milder cases; they have also been associated with dramatically increased prevalence rates and heightened public awareness and concern regarding this family of disorders. Efforts to identify causal factors have grown dramatically but continue to be complicated by the heterogeneous presentation of autism spectrum disorders. Continued advancements in diagnostic practices and descriptive capabilities are needed to define boundaries within this spectrum and to identify subtypes for treatment and etiological research.

The first two studies in this three-paper project suggest preliminary means to stratify this diverse population into more homogeneous subgroups by ASD severity in order to detect genetic and neurobiological similarities within more narrow groupings. The ability to quantify autism severity could contribute to research into possible causes and prognoses of these disorders, which ideally may come to impact prevention or treatment of future generations with ASD. In order to intervene positively in the lives of individuals currently living with ASD, however, it may be much more important to identify tractable factors affecting quality of life. The proportion of adolescents and adults with ASD and comorbid depression is much greater than that of depression in the

general population. The third paper in this series has implications about the targeted treatment of adaptive behavior skills as a means to prevent or treat depressive symptoms in adolescents and adults with ASD and thus improve quality of life for these individuals.

Severity of impairment in autism spectrum disorders is defined differently in relation to both autism-specific and comorbid factors; arguably, different definitions of impairment become more salient in the lives of individuals with ASD at different age periods. The three studies that comprise this dissertation represent steps toward measurement of autism-specific severity in children and adolescents and treatment of depression-related impairments in adolescent and adults. Further research on these topics will inform our use and revision of new measurement techniques and instruments described herein, and is needed to extend our understanding of these and many other possible definitions of "impairment" in autism spectrum disorders.