DEVELOPMENTAL CASCADE MODELS IN AUTISM SPECTRUM DISORDERS

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Abstract

Background: Developmental neuroscience research suggests that relative differences in emerging social skills between very young children with ASD may influence the trajectories of multiple important developmental domains, such as language ability. Such "cascade" associations between developmental trajectories may contribute in important ways to the substantial heterogeneity in symptoms and functioning seen in children with ASD. However, longitudinal research has yet to test such "cascade" models of change in children diagnosed with ASD.

Objectives: In this dissertation I aimed to model cascade patterns of association between social competence and language ability pathways in the year after diagnosis of ASD in preschool-aged children. Data for 365 participants aged 2-4 years old who had been recently diagnosed with ASD and followed prospectively were obtained from the "Pathways To Better Outcomes in ASD Study".

Methods: Study 1 aimed to determine whether social competence and structural language ability could be measured as distinct constructs that were invariant over time and between clinically relevant groups of young children with ASD. Study 2 modeled longitudinal reciprocal associations between these domains. Study 3 addressed the issue of variability and change within this sample, and tested whether baseline levels and rate of change in one domain were associated with subsequent growth in the other.

Results: Social competence and language ability constructs were measurably distinct and invariant in a young sample comprising verbal and non-verbal children with ASD. Only small reciprocal cascade effects were evident between social and language pathways. Levels of social competence at time of diagnosis were significantly associated with subsequent language growth.

Conclusions: In preschoolers with ASD, advantages in social competence as measured at time of diagnosis appear to “spill over” in a feed-forward cascade model to influence progress in language ability. Social competence and language ability then appear to develop along more specialized, less interrelated pathways.

Keywords: autism spectrum disorders, cascades, heterogeneity, reciprocal effects, latent growth curve models, language ability, social competence

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I also want to express my enormous gratitude to the children with whom I have had the privilege of talking and playing in clinic, on the courts and at camp, and who have been my first and best teachers.

This dissertation is dedicated to my parents, Elizabeth and Gerald Bennett, who are my models of passionate lifelong learning and to whom I owe all of this.

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List of Abbreviations and Symbols

ABC: Aberrant Behaviors Checklist
AC: Auditory Comprehension
ADI-R: Autism Diagnostic Interview- Revised
ADOS: Autism Diagnostic Observation Scale
APA: American Psychiatric Association
CELF: Clinical Evaluation of Language Fundamentals
CFA: Confirmatory Factor Analysis
CFI: Comparative Fit Index
Cog: Cognitive
D: Disturbance term
DSM-IV-TR: Diagnostic and Statistical Manual, Fourth Edition, Text Revision
E : Error Term
EC: Expressive Communication
EFA: Exploratory Factor Analysis
ICEPT: Intercept
IR: Interpersonal Relationships
IQ: Intelligence Quotient
IR: Interpersonal Relationships
IRT: Item Response Theory
LANG: Language Ability
LANG $_{1,2,3}$: Language Ability Measured at Times 1, 2 or 3
LGC: Latent Growth Curve
MI: Multiple Imputation
M-P-R: Merrill Palmer Developmental Scales Revised
M-P-R-CD: Merrill Palmer Developmental Scales Revised, Cognitive Domain Score
PCA: Principal Components Analysis
PDD-NOS: Pervasive Developmental Disorder Not Otherwise Specified
PLS-4/PLS4: Preschool Language Scale, Fourth Edition
PLT: Play and Leisure Time
RMSEA: Root Mean Square Error of Approximation
SC: Social Coping
SD: Standard Deviation

SE: Standard Error
SEM: Structural Equation Modeling
SOC: Social Competence
$SOC_{1\text{-}3}$: Social Competence Measured at Times 1, 2 or 3
SS: Standard Score
T1/T2/T3: Time 1/Time 2/Time 3
TL: Total Language
TLI: Tucker-Lewis Index
VABS-II: Vineland Adaptive Behavior Scales, Second Edition
VABSII-PLT: Vineland Adaptive Behavior Scales, Second Edition, Play and Leisure Time Subdomain Score of Socialization Domain
VABSII-SC: Vineland Adaptive Behavior Scales, Second Edition, Coping Skills, Subdomain Score of Socialization Domain
VABSII-SIR: Vineland Adaptive Behavior Scales, Second Edition, Interpersonal Relationships Subdomain Score of Socialization Domain
χ^2: Chi-Squared Test
$\Delta\chi^2$: Change in Chi-squared Test Value

Declaration of Academic Achievement

This 'sandwich thesis' consists of three studies conceived of and written by the student. She developed their rationale, objectives, designed and conducted their data analyses, prepared the manuscript and made revisions as recommended by the co-authors. All of this work was completed between January 1, 2008 and August 6, 2013. As such all the work contained herein meets the requirement for inclusion in the manuscript of the thesis. In keeping with the requirements of a 'sandwich thesis', I highlight the contributions made to each study by my co-authors.

Study 1 describes the discriminant validity and measurement invariance of longitudinal latent variable models of social competence and language ability in children aged 2-4 with autism spectrum disorders (ASD). It was co-authored by the following individuals: Dr. Peter Szatmari is the principal investigator of the "Pathways in ASD" Study, which provided data for these analyses. He also read the manuscript and made constructive suggestions. Dr. K. Georgiades, Dr. M. Janus, and Dr. S. Hanna reviewed the rationale and analyses during the development of the paper and offered constructive suggestions on the manuscript. Dr. S. Georgiades and Dr. E. Duku offered suggestions regarding the analytic approach and critically reviewed the manuscript. Dr. S. Bryson, Dr. E. Fombonne, Dr. I. Smith, Dr. P. Mirenda, Dr. J. Volden, Dr. C. Waddell, Dr. W. Roberts, Dr. T. Vaillancourt, Dr. L. Zwaigenbaum and Dr. M. Elsabbagh are co-principal investigators or co-investigators on the "Pathways" Study; they approved the rationale and design of this study and critically reviewed the manuscript. Ms. A. Thompson gave advice on the measures used and reviewed the manuscript.

Study 2 examines the reciprocal associations between the longitudinal pathways of social competence and language development in preschool-aged children with ASD. Dr. Peter Szatmari is the principal investigator of the “Pathways in ASD” Study, which provided data for these analyses. He also critically reviewed the manuscript. Dr. K. Georgiades, Dr. M. Janus, and Dr. S. Hanna reviewed the rationale and analyses during the development of the study and critically reviewed the manuscript. Dr. S. Georgiades and Dr. E. Duku offered suggestions regarding the study rationale and analytic approach and also reviewed the manuscript. Dr. S. Bryson, Dr. E. Fombonne, Dr. I. Smith, Dr. P. Mirenda, Dr. J. Volden, Dr. C. Waddell, Dr. W. Roberts, Dr. T. Vaillancourt, Dr. L. Zwaigenbaum and Dr. M. Elsabbagh are co-principal investigators or co-investigators on the “Pathways” Study; they critically reviewed the manuscript. Ms. A. Thompson provided advice regarding measurement and analysis.

Study 3 examines dynamic interactions between the growth trajectories social competence and language development in the same sample of young children with ASD and the extent to which such patterns differ between children with ASD with and without comorbid intellectual disability. Dr. Peter Szatmari is the principal investigator of the larger “Pathways in ASD” Study and read the manuscript and made constructive suggestions. Dr. K. Georgiades, Dr. M. Janus, and Dr. S. Hanna critically reviewed the manuscript. Dr. S. Georgiades and Dr. E. Duku offered suggestions regarding the analytic approach and critically reviewed the manuscript. Dr. S. Bryson, Dr. E. Fombonne, Dr. I. Smith, Dr. P. Mirenda, Dr. J. Volden, Dr. C. Waddell, Dr. W. Roberts, Dr. T. Vaillancourt, Dr. L. Zwaigenbaum and Dr. M. Elsabbagh approved the rationale and design of this study and critically reviewed the manuscript. Ms. A. Thompson gave advice on the measures used and reviewed the manuscript.

CHAPTER ONE

Background

Autism spectrum disorders (ASD) are complex, highly heritable neurodevelopmental disorders characterized by core impairments or differences in social reciprocity, communication and restricted interests, and/or repetitive, stereotyped behaviors. Estimates of prevalence indicate that 1 in 150 to 1 in 88 children will meet criteria for ASD (Fombonne, 1999; Kogan et al., 2009; Newschaffer et al., 2007). There is significant variability in the burden of core symptoms and co-morbid disabilities that individuals will experience over their lifetime: While on average, social reciprocity symptoms often improve over time, many individuals remain significantly socially impaired with significant cognitive and language disability. Others may demonstrate fewer core symptoms, yet become quite incapacitated by co-morbid psychiatric disorder or intellectual disability (Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008; Howlin, Goode, Hutton, & Rutter, 2004; Szatmari et al., 2009). A smaller number of individuals with ASD may be much more subtly impaired, and their differences may affect their functioning only in adolescence or adulthood during stressful transitions or when relationship difficulties occur (Cederlund, et al., 2008). Functional outcomes in autism spectrum disorders (ASD) also differ significantly across individuals over time: many continue to require significant clinical support in adulthood, whereas others progress toward independent living (Cederlund, et al., 2008; Howlin, et al., 2004).

Understanding which early risk processes explain such important variability over time is particularly crucial in the case of ASD, which has been characterized by greater heterogeneity in symptom burden and functional outcomes than is typically described in other developmental disorders (Mawhood, Howlin, & Rutter, 2000). After following a group of boys with autism into adulthood, Mahwood, Howlin & Rutter (2000) concluded: "…any proper understanding of the disorder will clearly require this (heterogeneity) to be taken into account". Parents, caregivers, researchers and policy-makers share a vested interest in better understanding how early risk and protective factors lead to more challenged versus more optimal outcomes. Estimating how children who have recently been diagnosed with ASD will fare over time with respect to burden of symptoms, co-morbidity, enjoyment of relationships and the ability to live independently helps parents anticipate their child's needs and plan accordingly. The reliable identification of a range of early indicators of outcomes also guides interventionists in the delivery of more targeted and effective interventions across the lifespan of individuals with ASD and aids policymakers to plan resources and care strategies more broadly at a population level.

In this dissertation, I will argue that any discussion of heterogeneity in ASD must be informed by epidemiology: in particular longitudinal observational methods and studies that are informed by developmental social neuroscience. ASD has been described as a syndrome of “multiple disordered trajectories” (Tager-Flusberg, 2010). This characterization has been supported by a recent succession of prospective longitudinal cohort studies, which demonstrate that children with ASD present with very different levels of symptoms and abilities by the time of diagnosis (Bryson et al., 2007; Tager-Flusberg, 2010) and develop at very different rates (Anderson et al., 2007; Anderson, Oti, Lord, & Welch, 2009; Siller & Sigman, 2008; Szatmari, et al., 2009). These epidemiological studies have yielded important information about early predictors of development, however they have tended to focus on one domain of development at a time (Anderson, et al., 2007; Anderson, et al., 2009).

Research in the field of ASD therefore lags behind other domains of inquiry within child development and mental health respect to understanding how changes in important developmental domains and contexts of the child influence each other over time (e.g. see Bornstein, Hahn & Suwalksi, 2013; Obradovic, Burt & Masten, 2010) . This requires longitudinal studies that model multiple trajectories simultaneously. Such studies, informed by developmental neuroscience, may show us how the development of early fundamental “upstream” abilities -- may amplify or constrain change in other pathways that are “downstream” in a child’s development.

New insights and directions from the cognitive neuroscience of ASD argue that greater understanding of developmental complexity is required to appreciate this dialectic of common early impairments and multiplicity of outcomes (Karmiloff-Smith, 1998, 2006; Thomas et al., 2009). Specifically early deficits or differences at the level of genes, brain, cognitions or behaviours of very young children with ASD may become amplified over time by influencing how other related developmental pathways unfold. Such interactions are often referred to as *developmental cascades*. This concept is not new to the fields of cognitive psychology and developmental neuroscience (Karmiloff-Smith, 2009; Mundy, Gwaltney, & Henderson, 2010; Wass & Karmiloff-Smith, 2010) and has more recently become part of the lexicon of clinical epidemiology (Dishion, Veronneau, & Myers, 2010; Masten & Cicchetti, 2010; Obradovic, Burt, & Masten, 2010). However, to my knowledge, cascade theories from the former have not been used to inform studies in the latter. This lack of integration is particularly striking in the field of developmental research in ASD, which has been greatly illuminated by each discipline. This dissertation will demonstrate how theories relating to developmental cascades may guide our understanding of heterogeneity of outcomes in ASD. In doing so, I will propose some conceptual and methodological models to test hypotheses about specific patterns of cascades at the level of children's cognitions and behaviours, using longitudinal data from a large prospective cohort of toddlers and preschoolers with ASD.

Chapter 1 provides an overview of the recent history of developmental theory in ASD, including an overview of neuroconstructivism and cascade theory. It will also review current knowledge of two particularly important developmental domains in ASD – social competence and language ability -- and describe how methods in longitudinal clinical epidemiology may be used to empirically validate cascade theories in ASD. Chapters 2, 3 and 4 comprise the body of research studies that test specific longitudinal models of developmental cascades in very young children with ASD. Finally Chapter 5 will review the study findings and their contributions to developmental theory and methodology in ASD research. It will also include a larger discussion of the promise and limitations of longitudinal epidemiology as a translational approach linking cognitive-developmental neuroscience and outcomes research. I will then discuss future directions for studies that build upon the hypotheses and findings outlined in this dissertation.

Chapter 1

Recent Theoretical Developments in Understanding ASD.

In the past decade, a major shift occurred in psychology and neuroscience research from the search for a “unifying deficit theory” of ASD to a more complex and developmentally informed approach. Theory of mind, executive dysfunction and weak central coherence have each been proposed as core deficits that may explain almost all of the other impairments in ASD (Baron-Cohen, 1991; Frith & Happe, 1994; Happe, 1999; Happe & Frith, 1996). Some developmental researchers have argued that such deficit models do not take development into account, nor do they attempt to explain the significant heterogeneity of ASD, in which multiple genetic and/or environmental “hits” appear to occur early in development (Dawson, Sterling, & Faja, 2010; Elsabbagh et al., 2011; Happe, Ronald, & Plomin, 2006; Tager-Flusberg, 2010).

Longitudinal research has tried to explain this heterogeneity by identifying early characteristics of children with ASD that appear to predict meaningful outcomes later in adolescence and adulthood. For example, early cognitive and language abilities appear to be robust predictors of diverse outcomes such as symptom burden and later adaptive functioning (practical abilities in social and communication skills and self-care) (Bennett et al., 2008; Howlin, et al., 2004; Szatmari, Bryson, Boyle, Streiner, & Duku, 2003; Venter, Lord, & Schopler, 1992). The achievement of fluent language (or lack of language impairment) and intellectual disability by age of 5-6 years has perhaps been most consistently related to outcomes across multiple studies (Bennett, et al., 2008; Howlin, et al., 2004; Rutter, Greenfeld, & Lockyer, 1967; Szatmari, et al., 2009). However, a recent prospective longitudinal study has also found that childhood social reciprocity was strongly related to a composite of adult outcomes (including employment, relationships and independent living) (Howlin, Moss, Savage & Rutter, 2013).

Identifying early predictors is an important task in longitudinal research, but we also need to ask “how” or “why” predictors such as early language ability are associated with variation in outcomes such as adaptive functioning. From a theoretical perspective, constraints or growth in one developmental domain may influence change across other important domains, especially if they are linked in brain development (Elsabbagh, et al., 2011; Kuhl, Coffey-Corina, Padden, & Dawson, 2005; Mundy, Sigman, & Kasari, 1990). For example, research suggests that children with ASD may use their language skills to understand social situations to a greater extent than do same-aged typically developing peers (Fisher, Happe, & Dunn, 2005). The additional burden of language impairment in children with ASD may therefore further constrain their social development. Conversely one domain may facilitate another by opening up new opportunities for growth. For example, in linguistically higher-functioning children, better language skills may facilitate more opportunities for social interaction, which in turn may lead to better social skills.

Neuroconstructivism and Developmental Cascade Theories

"Neuroconstructivism" (Karmiloff-Smith, 1998; Sirois et al., 2008) is a particularly promising theoretical framework that can capture this dynamic interplay between developmental domains, and it has gained increasing recognition in cognitive and developmental neuroscience research. The neuroconstructivist approach emphasizes that the developmental process itself is fundamental to understanding developmental disabilities (Farran & Karmiloff-Smith, 2012; Karmiloff-Smith, 1998, 2009; Sirois et al., 2008). This entails moving away from static comparisons of brain regions as either "impaired or intact" (Karmiloff-Smith, 1998). Instead neuroconstructivism emphasizes how early differences -- genetic alterations, environmental exposures, brain trauma-- may constrain cognitive-developmental trajectories over time and have cascading effects over multiple other developmental and/or behavioral pathways (Farran & Karmiloff-Smith, 2012; Karmiloff-Smith, 1998; Thomas, et al., 2009). To date, longitudinal studies of development and psychopathology have focused mainly on how cross-sectional measures of abilities or trajectories of individual ability domains (e.g. language) differ *between* groups of children (e.g. ASD vs. typically developing or developmentally delayed control groups). Neuroconstructivism emphasizes how changes in different developmental domains interact over time, and the extent to which the strength of such associations differ within individuals; thus, it offers a particularly promising framework for understanding how differences arise between children with ASD with respect to core symptoms and associated cognitive, linguistic and psychiatric disability– that is, the heterogeneity of the ASD phenotype.

More specifically to the study of developmental disabilities, neuroconstructivism may further our understanding of variation in outcomes by emphasizing how the trajectories of different developmental domains diverge or influence each other *within* children as individuals. For example, differences in the pattern or strength of associations between developmental domains over time may distinguish specific syndromes such as ASD from children with other developmental or psychiatric profiles (Thomas, Purser, & Van Herwegen, 2012). These may reflect atypical underlying neurodevelopmental processes or compensatory strategies. For example, phonological awareness is a consistent predictor of later reading ability in typically developing children, but does not appear to be associated with reading level in children with Down Syndrome or Williams Syndrome (Hulme et al., 2012; Muter, Hulme, Snowling and Stevenson, 2004; Steele, Scerif, Cornish and Karmiloff-Smith, 2013). A neuroconstructivist approach would therefore enhance longitudinal research in ASD by underscoring a more complete and dynamic understanding of the developmental processes that occur in the causal chain between predictors and outcomes.

Understanding how cascade patterns may underlie developmental psychopathology has become more widely studied in child mental health research, particularly in relation to child behaviors or competencies and contexts such as families, peer groups and schools (Gross, Shaw, Moilanen, Dishion, & Wilson, 2008; Marsh, Gerlach, Trautwein, Ludtke, & Brettschneider, 2007; Marsh & O'Mara, 2008; Veronneau, Vitaro, Brendgen, Dishion, & Tremblay, 2010; Wang, Dishion, Stormshak, & Willett, 2011). As researchers uncover new information about the genetic, neural, cognitive and behavioural underpinnings of developmental and psychiatric disabilities across the lifespan, developmental scientists have focused increasingly on how functioning in one "domain or level or system influences another system or level of function over time" to better understand the underlying causal mechanisms and course of impairment or illness in developmental and psychiatric disorders (Masten & Cicchetti, 2010, p. 491). Masten & Cicchetti (2010, p.491) defined cascade patterns as,

> Processes that refer to the cumulative consequences for development of the many interactions and transactions occurring in developmental systems that result in a spreading across levels, among domains at the same levels, and across different systems or generations.

An example of cascades between systems may include child and caregiver: Children who begin to engage their parents in joint attention by pointing out an object of interest (e.g. an airplane in the sky) may elicit greater caregiver enthusiasm for naming and pointing in turn, which may then reward the child further and draw out more of the same behaviors. Cascades may also occur at one level, e.g. at a cognitive level when a child develops one skill (e.g. grasping) that opens up learning in other abilities (e.g. understanding intentional movement) (Sommerville, Hildebrand, & Crane, 2008). Cascades may therefore be positive, as the development of competences in a given domain or level facilitates the positive growth of further competencies (Cicchetti & Masten, 2010). Cascades may also be negative, when initial disadvantages act as important constraints across other developmental trajectories: children who are delayed or impaired in particular domains (e.g. late language acquisition due to congenital hearing impairment) then fall further behind across other domains of development (e.g. theory of mind; Peterson & Siegal, 2000).

Interactions between developmental domains over time may differ with respect to overall patterns as well. Reciprocal cascades describe abilities or behaviours that build off each other in a back-and-forth manner over time. In some cases, such cascade patterns are synonymous with processes that are well-described in the developmental psychology literature, such as scaffolding or bootstrapping, in which advantages or learning in one domain enable further development in another which in turn feeds back to further development in the first domain (Karmiloff & Karmiloff-Smith, 2001). Cascades may also feed-forward more unidirectionally, for example as advantages in one domain initiate or magnify growth in another without an obvious reciprocal feedback effect. For example, phonological awareness appears to influence reading growth during the first year of reading in typically developing children, however does not appear to be strongly related later in preschool and school-aged years during which time literacy skills appear to build on themselves (Muter, Hulme, Snowing & Stevenson, 2004). In both patterns, initial upstream advantages or disadvantages may amplify or constrain multiple developmental pathways.

Cascade effects may differ by developmental time, as well. Certain abilities may build on each other during one critical period but not another, for example because of developmental differences in the specialization or connectivity of brain regions (e.g. infancy versus adolescence), or because of shifts in environmental contexts (preschool versus school) (Johnson, 2007; Masten & Cicchetti, 2010). Furthermore, some associations may occur only in the short-term, or over a longer period of time.

Applying the concept of developmental cascades to hypothesis-testing and study design in longitudinal child development and psychopathology research is important for several reasons: First, such "pivotal skills" (Charman, 2003) may be more strongly and specifically associated with growth in other important developmental domains than are other early-emerging abilities, or they may exert a more pluripotent effect across a wider range of downstream abilities. Identifying potentially higher-impact developmental domains for a given developmental period from toddlerhood to adolescence and targeting these preferentially should yield more optimal early intervention. Second, understanding whether certain domains are more strongly linked in the developmental psychopathology of certain syndromes compared to others (e.g. Williams Syndrome vs. ASD) may lead to improved tailoring of cognitive and behavioural interventions to specific groups of children. Finally, understanding how the trajectories of developmental domains relate to each other over time, and whether such associations differ between developmental time periods (e.g. toddlerhood vs. preschool vs. school-aged vs. adolescent years) will help to target sensitive periods for specific developmental processes. For example, during the preschool years (in both typically developing and disabled children) social, cognitive or language processes may influence a number of subsequent developmental pathways, whereas the emergence of mental health problems may be a more important constraint on specifically adolescent developmental tasks such as self-awareness, independence and the formation of lasting relationships outside of the family .

Developmental cascades, therefore, may be particularly important to unlocking the processes that link risk factors to outcomes in studies of individuals with ASD. However, significant longitudinal research using large, representative samples of children with ASD (and other developmental disabilities) in order to test specific cascade models is lacking. Many neuroconstructivist studies estimate developmental pathways by using cross-sectional experimental designs. For example, trajectories may be constructed by using data from case- and control participants across a range of chronological or mental ages. These are then used to estimate how patterns of growth in particular developmental domains (e.g. language, attention) differ between children with disabilities and controls (Thomas, Purser and Van Herwegen, 2012).

Such studies are essential, however they require further empirical validation using true prospective studies and representative samples of children with particular developmental disabilities. In contrast to cross-sectional designs, longitudinal research aims to describe the process of developmental *change* within individuals. Such studies must therefore include: a) follow-up of a representative sample of children (with or without control groups) assessed over multiple time points and b) repeated reliable, valid measures of the developmental constructs of interest, that are sensitive to intra-individual change between- and across all time points of interest. More specifically, longitudinal cascade models describe two or more paths or trajectories representing constructs of interest (e.g. specific developmental domains such as language, cognitive or motor development) measured over time, as well as paths representing associations between each domain over multiple time points -- usually within-time (at the same time point) and prospective associations (from one domain to another at a later time point). Hypothesized cascade models are then often compared to competing alternative models. Longitudinal cascade models are correlational and cannot prove causation, however carefully designed studies of this kind may provide empirical support for a particular cascade theory as a plausible developmental process. Further longitudinal studies may then refine such models, for example by replicating a model in different samples, using different measures, or testing other competing models.

In this manner, longitudinal research and developmental neuroscience may inform each other and contribute to a broader and deeper understanding of developmental questions in a form of iterative loop: Cognitive-developmental- and neuroscience research can provide important important testable hypotheses about longitudinal cascade mechanisms that refine prospective cohort study designs. Longitudinal studies and analytic approaches may then test the extent to which cascade associations are measurable over time at the “real-world” level of child cognitions and behaviours. This in turn may inform the field of intervention research and feed new insights back to the fields of cognitive psychology and developmental neuroscience for further exploration of genetic, neural or cognitive processes at a more detailed level.

Social competence and language are particularly compelling domains for beginning to understand developmental cascades longitudinally in studies of children with ASD. From a cognitive development and neuroscience perspective, early emerging social attunement and engagement in interactions appear to be pivotal skills that influence the emergence and development of language abilities (Charman, 2003; Kuhl, Coffey-Corina, Padden & Dawson, 2005; Mundy, Sigman & Kasari, 1990; Siller & Sigman, 2008). These are core, or common, deficits of ASD, yet there is evidence that heterogeneity exists – at the time of diagnosis, children vary considerably with respect to the extent of their social and language impairment (Anderson, et al., 2007; Anderson, et al., 2009; Kuhl, Coffey-Corina, Padden, & Dawson, 2005; Siller & Sigman, 2008; Szatmari, et al., 2009). As discussed above, early language ability has been identified as a primary prognostic factor within epidemiology research involving various cohort studies of children who differ by age and severity of ASD. This dissertation will attempt to test, using longitudinal analytic methods, the developmental cascade models of social competence and language in a prospective cohort sample of 2-4 year-old children with ASD over the 12 months after the time of diagnosis. More specifically, I will demonstrate how developmental theories of ASD may be utilized to build hypotheses that may be tested in longitudinal structural equation models.

Review of Social and Language Development in Children With and Without ASD

In these chapters, *social competence* refers to the extent to which children demonstrate skills in age-appropriate levels of social interest, social-cognitive skills and effective pro-social behaviours. *Social interest* refers to a child's essential motivation to orient towards others – e.g. a typically developing infant's apparently reflexive looking towards faces – and to seek out social interactions. *Social cognition* entails the thought processes that underlie how we process social stimuli and interact effectively with others; this includes such functions as looking at faces, following eye gaze, decoding body language and anticipating movement, reading facial expressions and inferring the thoughts and intentions of others (i.e. theory of mind) (Baron-Cohen, 1991; Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Premack & Woodruff, 1978). Paper-and-pencil or laboratory-based measures are often used to assess a child's social-cognitive abilities, such as asking the child to infer a cartoon character's thoughts (Brent, Rios, Happe, & Charman, 2004; Jolliffe & Baron-Cohen, 1999; White, Hill, Happe, & Frith, 2009). *Pro-social behaviors* may include a child's engagement in a peek-a-boo game, or their response to distress demonstrated by an examiner. Parents may report on a child's behaviors and inferred social-cognitive ability in questionnaire format (Constantino et al., 2003) or interview (e.g. the Social Subscales of the Vineland Adaptive Behavior Scale or VABS-II (Sparrow, Cicchetti, & Balla, 2005). Such assessments may infer social-cognitive abilities indirectly (e.g. whether a child is able to recognize others' emotions) and social behaviors more directly (e.g. whether a child responds to others' distress).

Emerging Social Competence in Typically Developing Children.

The earliest building blocks of social competence emerge during the first days of life. At a neural level, there is evidence that very young infants preferentially "tune into" other humans and faces, which may indicate that subcortical routes for reflexively directing attention to social stimuli – inherent reward pathways – are present by the time of birth (Carver & Cornew, 2010; Johnson et al., 2005). According to Johnson (2005), as children gain experience through social interactions, the roles and responses of brain structures to social stimuli gradually become more specialized and differentiated during childhood.

At the level of cognition and behavior, social competence also appears to emerge in the first days of life in typically developing infants (Carver & Cornew, 2010; Grossman & Farroni, 2009). Shortly after birth, infants prefer face-like features over other stimuli and can detect eye gaze in certain situations (Grossman & Farroni, 2009). Joint attention – the ability to coordinate attention with another person on a third object or person, as demonstrated by pointing or following eye gaze – is considered to be a seminal early social skill (Mundy & Jarrold, 2010) that develops most obviously between the ages of 10-13 months (Grossman & Farroni, 2009; Sigman, Mundy, Sherman, & Ungerer, 1986). Infants as young as 18 months old begin to understand the intentions of others based on their behaviours (Meltzoff, 1999), and children most clearly gain an understanding of false belief (that other individuals can believe or know something that the child knows to be false -- a hallmark test of theory of mind) between the ages of 3 and 4 years (although possibly earlier) (Carver & Cornew, 2010).

Emotion recognition, empathy and prosocial behaviors are also essential milestones in the development of social competence. Typically developing infants become expert at recognizing specific emotions prior to their first birthday and then continue to hone this skill set throughout their preschool and school-aged years as they detect more nuanced facial and behavioural cues (Carver & Cornew, 2010). Imitation may be an important developmental precursor of empathy, and also emerges early, as evidenced when newborns appear to mimic human interaction (Decety & Meyer, 2010). Empathy refers to the affective response that stems from an understanding and the sharing of another person's emotional state; like theory of mind, it appears to develop more fully between the ages of 2 and 4 years old (Decety & Meyer, 2010; Eisenberg, 2000). Empathy-driven responding appears to precede prosocial behaviours such as responding to others' distress, helping and sharing, which become more fully developed by age 4 (Zahn-Waxler & Radke-Yarrow, 1984).

Language Development in Typically Developing Children.

The infancy-to-preschool period is perhaps equally important to optimal language development: While a thorough examination of human linguistic development is beyond the scope of this chapter, a basic understanding of the developmental timeline for receptive and expressive language is important to an understanding of the associations of language with emerging social competence. Most simply, receptive language is comprised of the ability to comprehend gestural and spoken language, while expressive language refers to the effective production of language through facial expression, gestures and speech. Structural language refers to the elements involving vocabulary and syntax, and includes an understanding and ability to use gestures and to learn words and increasingly complex grammatical units in order to communicate with others. Pragmatic language involves the more inherently social use of language within communication, such as an ability to converse with others skillfully with others and to use social information to contextualize the meaning of gestural or spoken language (Karmiloff & Karmiloff-Smith, 2001).

Among typically developing children, changes occurring during the first year lay the developmental foundations for receptive and expressive language. Children typically begin to babble around 6 months of age, then begin gesturing and demonstrating their receptive language skills around age 9 months. By 12 months of age, typically developing children begin generating some words, followed by a vocabulary “explosion” of 50-100 words learned between the ages of 18-20 months (Nelson, 2007). The combined use of gestures and words appears to form a platform for the development of multiword speech and more complex grammatical understanding that typically occurs during the third year of life. By age 3, many children are becoming increasingly skilled conversationalists, with a more refined awareness of others’ points of view and a greater understanding of pragmatic language (Shatz, 2007).

Interactive Pathways in Social Competence and Language Skills: Typically Developing Children.

The early interdependence of social and language skills are important examples of developmental cascades. The developmental trajectories of social competence and language abilities in typically developing children are usually defined as separable pathways. However, cognitive-developmental research has consistently highlighted their inter-relatedness, particularly in the early preschool years of childhood. Many researchers hypothesize that developmental cascades occur in a “boot-strapping” pattern, such that skills in one domain scaffold learning in another (Akhtar & Martinez-Sussman, 2007; Nelson, 2007; Shatz, 2007). However, there is a dearth of longitudinal research modeling social and language pathways simultaneously, with most studies instead relying upon a risk-factor outcome model (i.e. 2 time points).

Experimental and longitudinal research to date supports the importance of early social competence to emerging language skills, in that: 1) joint attention is an important precursor of language development (Mundy & Jarrold, 2010; Siller & Sigman, 2008); 2) social interactions with caregivers (as compared to video-recorded or computer-generated stimuli) are pre-requisites of language learning among infants in their first year (Kuhl, 2010; Siller & Sigman, 2008); 3) children are strongly motivated to listen in on others' conversations and thereby learn new words, even when they are engaged in other activities (Akhtar & Martinez-Sussman, 2007). Therefore, some degree of social competence and motivation appears to be fundamental to word-learning during the first 2-3 years of life. There have been relatively few studies of the influence of social factors on grammar development; however, in comparison to word-learning, more complex grammatical understanding is thought to rely less upon concurrent social skills (Akhtar & Martinez-Sussman, 2007).

Language in turn, is considered by many researchers to be an important prerequisite of further gains in social competence, however there have been relatively fewer studies examining associations in this temporal direction. Longitudinal follow-up of 3 year-olds found that structural language abilities predicted later skills in theory of mind, but baseline theory of mind at age 3 did not predict later language (Astington & Jenkins, 1999). More specifically, children may require certain prerequisite grammatical skills in order to grasp advanced theory of mind concepts such as false-belief (the notion that another person can believe a mistaken thought, that is also different from one's own) (De Villiers & Pyers, 2002). Delays or impairment in acquiring structural language can also constrain social competence pathways: Children with non-ASD specific language impairment (SLI) have been shown to have impairment in social-cognitive abilities or social outcomes such as quality or number of friendships (Cohen et al., 1998; Howlin, Mawhood, & Rutter, 2000). Similarly children who are profoundly hearing impaired, and are delayed in learning sign language demonstrate delays or deficits in the social skills and the quality of their play (De Villiers, 2005).

Emerging Social Competence in Children with ASD.

The unfolding psychopathology of ASD may largely be characterized as pathways in social and linguistic development that have gone awry (Tager-Flusberg, 2010). Brain biomarker research in baby siblings of children with ASD (i.e. “high-risk baby sibs”) suggests that early atypicalities may develop in the cortical specialization of specific brain regions in children with ASD, reflecting differences or deficiencies in the social networks of the brain (Elsabbagh & Johnson, 2010; Johnson, et al., 2005). Such neural changes are thought to occur between the ages of 8-12 months. According to follow-up studies of high-risk siblings of children with ASD (i.e. in “baby sibs” studies), behavioural changes may also begin to appear during this time. Prospectively identified differences are not obvious before 12 months of age however in one study, a subset of children who were diagnosed with ASD at age 24 months were found to have demonstrated differences with respect to responding to name when 6 months old (Zwaigenbaum et al., 2005). By 12 months of age, atypical social behaviors or delays appear to emerge with respect to eye contact and visual tracking, disengaging attention, orienting to name, imitating others, social smiling and social interest, reactivity and engagement with others (Bryson, et al., 2007; Werner, Dawson, Osterling, & Dinno, 2000; Zwaigenbaum, et al., 2005). Other related atypicalities have been demonstrated at 12-14 months, including increased involvement in sensory-oriented behaviors, differences in fine and gross motor abilities and more global impairment in general intelligence and early learning (Flanagan, Landa, Bhat, & Bauman, 2012; Landa & Garrett-Mayer, 2006; Zwaigenbaum, Bryson, & Garon, 2013).

Although valid and reliable behavioral markers of autism in infants and toddlers younger than 18 months old remain relatively elusive, there is general consensus that the early social developmental trajectories in children with ASD deviate from those of typically developing children (Dawson, et al., 2010; Elsabbagh, et al., 2011; Tager-Flusberg, 2010). Dawson's Social Orientation Theory of ASD proposes that deficits in the interest and/or ability to "tune into" others and to find the earliest social interactions to be rewarding are pivotal early social-cognitive and behavioral differences in children with ASD (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Dawson, et al., 2010). Constraints in the ability of children with ASD to engage in their social environment and develop other skills that would enlarge such environments (e.g. language and conversation, peer interactions and self-regulation) in turn limits further social development (Dawson et al., 2010). According to Dawson et al.

(2010), the extent of disability in social orientation of infants at risk for ASD may then determine other early-emerging and fundamental impairments in preschool children with ASD such as atypical face-processing (Klin & Jones, 2008); delayed or infrequent engagement in joint attention (Charman, 2003; Dawson, et al., 2010; Mundy, Sigman, Ungerer, & Sherman, 1986); difficulty with imitation, particularly spontaneous social imitation (Charman et al., 1997; Dawson, Meltzoff, Osterling, & Rinaldi, 1998; Smith & Bryson, 2007); and decreased prosocial behaviors, such as noticing and attending to others who are in distress (Bacon, Fein, Morris, Waterhouse, & Allen, 1998; Dawson, Meltzoff, Osterling, & Rinaldi, 1998; Dawson et al., 2004). Differences in social engagement and reciprocal interactions then constrain development in other domains such as language (Dawson, Meltzoff, Osterling, Rinaldi, et al., 1998; Mundy, et al., 1990).

Language Development in Children with ASD.

There is strong consensus that impairment in social, back-and-forth communication using gestures and speech is a core symptom of ASD. There is also increasing agreement among researchers and clinicians that many elements of structural language are also quite commonly impaired in children and adolescents with ASD (Tager-Flusberg & Caronna, 2007). Communication skills rely on many elements of language and in particular emphasize the importance of pragmatic language – the ability to use words and sentences in a variety of contexts in a socially appropriate manner, such as narrating a story, following rules of politeness, taking turns in conversation to listen and respond. Pragmatic language deficits are considered to be universal across individuals with ASD (Tager-Flusberg & Caronna, 2007; Volden, Coolican, Garon, White, & Bryson, 2009). For example, preschoolers with ASD will often use language for operational reasons, such as labeling, requesting or protesting rather than for social reasons such as sharing attention or commenting (Dawson, et al., 2010; Tager-Flusberg & Caronna, 2007).

Structural language development is also frequently compromised in children and adults with ASD, although abilities vary significantly across the autism spectrum (Anderson, et al., 2007; Bennett, et al., 2008; Caronna, Milunsky, & Tager-Flusberg, 2008; Eigsti, Bennetto, & Dadlani, 2007). Tager-Flusberg & Coronna (2007) estimated that only about 25% of individuals with ASD were able to achieve at least average scores on grammatical tests. In general, receptive language skills (comprehension) lag behind expressive abilities in children with ASD, contrary to the general pattern of typical child language development (Hudry et al., 2010; Volden et al., 2011). This may reflect difficulties in integrating language with real-world knowledge (Tager-Flusberg & Coronna, 2007). However the expressive skills of children with ASD, and their precursors, are often qualitatively atypical or quantitatively reduced, including fewer nonverbal gestures that typically precede language (Mitchell et al., 2006), atypical babbling and vocalizations such as repetitive screeching, moaning, humming, echolalia (repeating words/phrases in a nonfunctional manner), neologisms (making up new words) and persistent grammatical errors such as pronoun reversal (Tager-Flusberg & Caronna, 2007).

Associations between Social Competence and Language Pathways in ASD.

The overall pattern of associations between social competence and language among children with ASD may be more similar than different in comparison to patterns of typical child development: As in typically developing children, in very young children with ASD there is preliminary evidence that relative impairment or strength in emerging social competence may constrain or facilitate language development (Dawson, et al., 2004; Kuhl, et al., 2005; Mundy, et al., 1990). The main difference, perhaps, is that children with ASD, on average, demonstrate much poorer emerging social competence compared to typically developing and developmentally delayed peers.

In keeping with Dawson's Social Orientation Theory, the reduced attention to social stimuli demonstrated by children with ASD appears to result in a failure to develop expertise in language processing (Dawson, Meltzoff, Osterling, Rinaldi, et al., 1998). For example, Kuhl and colleagues (2005) demonstrated that children with autism at ages 3-4 generally preferred computer-generated mechanical-sounding auditory stimuli to spoken human language, an inclination that differed significantly from typically developing children. However, within the group of children with ASD there was variability in the strength of this tendency: those who preferred computer-generated sounds later demonstrated poorer language and more severe ASD symptoms (Kuhl, et al., 2005). ASD-specific deficits in joint attention appear to constrain language-learning, possibly related to a dissociation between gaze-following and intention-reading in children with ASD (Charman, 2003; Gliga, Elsabbagh, Hudry, Charman, & Johnson, 2012; Mundy, et al., 1990; Parish-Morris, Hennon, Hirsh-Pasek, Golinkoff, & Tager-Flusberg, 2007).

Language impairment may also be an important constraint on the development of more advanced social skills among children with ASD. A child’s difficulty in detecting and decoding language stimuli such as gestures and speech may prevent the requisite specialization of social-cognitive regions of the brain region, which in turn would lead to slower processing speed of social stimuli and impaired social behaviours (Dawson, Sterling & Faja, 2009). As with typically developing children, studies have not incorporated social and language trajectories simultaneously in longitudinal research designs in order to test cascades. Instead, cross-sectional research has suggested that language may be more strongly associated with theory of mind development in children with ASD: children with greater structural language skills appeared to compensate for social-cognitive deficits by verbally reasoning through scenarios in order to decode their understanding of others' thoughts (Fisher, et al., 2005). In a longitudinal study, structural language at age 6-8 years of age was found to be associated with theory of mind skills at age 12 in a cohort of 35 more cognitively capable children (IQ > 70; Bennett et al., 2013). Furthermore, children with ASD who have stronger receptive and expressive language skills also appear to demonstrate stronger play skills and have more successful social interactions, which suggests that language abilities may mediate their development of play (Tager-Flusberg & Caronna, 2007).

Testing Developmental Cascades: Social Competence and Language Ability in Very Young Children with ASD

Cognitive-developmental research and theory suggest that developmental cascades occur over time between social competence and language development in preschool-aged children. Social competence is an important early facilitator of language development in children, and an important early constraint among those in whom it is impaired. Language ability, in turn, may influence further development of more sophisticated social cognitive skills and behaviors.

The set of studies outlined in this dissertation aim to develop and test longitudinal cascade models of development in very young children with ASD. Data were obtained from the "Pathways in Autism Spectrum Disorders" study. The Pathways study is the largest longitudinal study of an inception cohort of young children with ASD in the world. Data have been collected from 5 sites across Canada (Halifax, Montreal, Hamilton, Edmonton and Vancouver). In total, 423 children between the ages of 2 and 5 joined the study within 4 months of their diagnosis of any ASD and will be followed to age 11. During the first phase of the study, children and parents participated in a battery of assessments that included questionnaires and psychometric tests at baseline, 6 and 12 months, and again at age 6 prior to transitioning to school. The Pathways Study incorporates multiple measures of child and contextual variables repeated over multiple time points during developmentally sensitive periods: Therefore it is ideally suited, methodologically, to testing developmental cascade models in a representative sample of children with ASD. The three chapters in this dissertation describe studies using the data available to date for 365 participants who had completed the first three time points: baseline (within 4 months of diagnosis of ASD) and 6- and 12-months post-diagnosis. More specifically, each chapter addresses issues in measuring developmental cascade models of change incorporating two important developmental pathways in children with ASD: early social competence and language ability.

The first chapter, "Longitudinal Measurement Models of Social Competence and Language Ability in Preschool-aged Children with ASD" establishes the methodological groundwork for the following two chapters by determining valid longitudinal measurement models for the developmental constructs of social competence and language ability in young children with ASD. In order to measure cascade patterns that occur at the same level – e.g. differing cognitive or developmental abilities within the same child that may influence each other over time – it is particularly important to first determine that such abilities may be measured as distinct constructs.

The second chapter is entitled, "Do Reciprocal Associations Exist Between Social and Language Pathways in ASD?". Developmental theories of emerging social and language skills – such as Social Orientation Theory (Dawson et al., 1998) -- suggest that the two domains may build on each other in a reciprocal pattern over time, as children use their abilities gained in one domain to scaffold skills in the other. This chapter tests this specific pattern of *reciprocal cascades* more explicitly by using a structural equation modeling (SEM) approach -- specifically, a cross-lagged auto-regressive reciprocal effects model to determine whether, in the same cohort of children aged 2-4 with ASD, levels of social competence at one time point predict levels of language at the next, and whether language ability in turn then predicts later social competence at a third time point.

The third chapter “Developmental Cascades in ASD: A Longitudinal Latent Growth Curve Model” builds upon the second by testing a different, and complementary approach, to testing cascade patterns: Using a dual-domain latent-growth curve model (an extension of SEM), this study tests a *feed-forward cascade* model to determine whether baseline abilities and/or growth in one domain spills over to influence *growth* in another. The analyses in this study discern the extent to which children in this sample vary from each other with respect to baseline levels and growth in social competence and language and whether baseline levels and gains made in social competence affect the rate of change in language ability over the course of the year after diagnosis of an ASD.

The aim of this dissertation is to explore the importance of developmental cascades as potential contributors to the heterogeneity of phenotypes, co-morbidity and outcomes within individuals with ASD. These studies do not address the specificity of such patterns to ASD, as they do not include a comparison control group of typically developing or developmentally delayed children for this cohort. Furthermore, the Pathways Study was designed to describe a group of children after the time of diagnosis of ASD rather than for the purpose of capturing the emergence of specific developmental abilities (i.e. first-emerging social competence or language). During the period of 12-month follow-up in the Pathways Study, many of the children demonstrated important initial social and linguistic milestones and developmental shifts, for example from no joint attention to demonstrated joint attention, from no words spoken to some words spoken. Others had already attained these skills and still more may not have attained them by the third time point. Therefore this study cannot fully test Dawson's (1998) theory of Social Orientation as it applies to the earliest-emerging social and linguistic skills of each child. However, these analyses can test the extent to which principles of Social Orientation Theory apply in already-diagnosed children with ASD, the majority of whom are delayed in both social and language domains.

The methodological strengths and sample size of the Pathways in ASD Study are ideally suited to testing cascade models during a period of important growth in social competence and language skills in preschool-aged children. Models such as these facilitate our understanding of the multiple developmental trajectories underlying the heterogeneity of symptoms and function in ASD, and whether variation in outcomes (e.g. "better" versus "worse" outcomes over time) are related to differences in how these trajectories are related to each other over time. The ultimate promise of such research is to identify highest-yield therapeutic intervention targets that are tailored to children's developmental profile – targets that will yield cascading benefits to children and adults with ASD.

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CHAPTER TWO

Study 1

Title: Emerging Social Competence and Language Ability in Preschoolers with Autism Spectrum Disorders: A Longitudinal Measurement Model

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Context and Implications: Impairments in social competence and communication are common and overlapping in children with autism spectrum disorders (ASD). In fact, the recently updated Diagnostic and Statistical Manual-5 has collapsed the two domains into one clinical construct of social-communication impairment. Research studies using a factor-analytic to examine the ASD phenotype generally support the argument that social and communication skills represent a common domain of impairment.

Many children with ASD also demonstrate structural language impairment -- co-morbid disability in the “non-social” aspects of language such as grammatical understanding. Such language ability/disability is considered to be one of the strongest predictors of functional outcomes in children with ASD and is now described in the DSM-5 as an important clinical specifier of the diagnosis. Furthermore, social competence and language ability appear to be inter-related in typically developing children and individuals with ASD but research that models both developmental pathways simultaneously over time is lacking. Longitudinal dual-domain studies of social competence and language first require a determination of the extent to which social competence/impairment and language ability/disability may be measured as a distinct constructs.

Using confirmatory factor analysis of commonly used social and language development measures and data from 365 children aged 2-4 with ASD, I concluded that these domains may be measured as distinct developmental constructs. Furthermore, the measurement properties of these instruments did not vary significantly over the course of 12 months or between children with and without comorbid intellectual disability. This study formed the basis for Studies 2 and 3 which then modeled cascading interactions between social competence and language in the same sample of children. It also lends support to the DSM-5 model that structural language impairment, as compared to more the social use of language defined as communication skills, may be measured as a related but distinct developmental ability among children with ASD.

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ABSTRACT

Previous autism spectrum disorders (ASD) research suggests that social- and communication skills represent a single developmental construct, however whether early social competence (SOC) and structural language (LANG) are measurably distinct is unclear. We examined the distinctive validity and measurement invariance of SOC and LANG in a sample of 365 children aged 2-4 with ASD, using the Vineland-2 socialization score and Preschool Language Scale-4 (baseline, 6- and 12 months). Confirmatory factor analyses indicated that SOC and LANG were measurably distinct. Measurement invariance was established in children differing by age at diagnosis and cognitive ability. Social competence and language skills may be measured as distinct but related developmental abilities, even in very young children with ASD.

INTRODUCTION

Autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by impairment in social reciprocity and communication, as well as patterns of repetitive, ritualistic behaviors or intense interests. Despite these common core features, ASDs are characterized by considerable heterogeneity in symptom severity and associated impairment in other domains of development, such as general cognitive ability, language skills and adaptive behaviours.

Structural language (as in grammar and vocabulary) and social competence are relevant to later meaningful outcomes such as adaptive functioning (Anderson et al., 2007; Anderson, Oti, Lord, & Welch, 2009; Bennett et al., 2008; Szatmari et al., 2009), so it is particularly important to characterize their patterns of change with considerable detail during preschool development. This might involve measuring these constructs at frequent intervals during a short duration of time to capture change during key periods. It is also important to measure how developmental abilities such as social competence and language interact over time in very young children with ASD, to understand both how development in ASD may relate to typical child development, and how to plan for targeted interventions. Emerging social abilities such as joint attention have been shown to predict language development (Anderson et al., 2007; Charman, 2003; Siller & Sigman, 2008), and verbal abilities also appear to influence social adaptive behavior trajectories (Anderson, et al., 2009).

This close inter-relationship between language and social competence raises the issue of whether the two represent a more fundamental domain of social-communication. This is particularly relevant because several recent studies examining the factor structure of the ASD phenotype using confirmatory factor analysis and other methods have not found social abilities and *communication* (defined as the social use of language) skills to represent distinct factors (Boomsma et al., 2008; Frazier, Youngstrom, Kubu, Sinclair, & Rezai, 2008; Georgiades et al., 2007; Gotham, Risi, Pickles, & Lord, 2007; Snow, Lecavalier, & Houts, 2009; Van Lang et al., 2006), with some exceptions (Lecavalier, Gadow, DeVincent, Houts, & Edwards, 2009). This has not been tested, however, using more specific or "pure" language measures, as opposed to communication measures which focus on pragmatic rather than the structural aspects of language. Even language measures that assess the structural aspects of language may overlap with measures of early social competence in younger or less cognitively developed children with ASD -- for example both may assess early joint attention skills such as pointing or gaze-following. It is therefore important to determine whether it is possible to distinguish between social competence and language between the ages of 2 and 4, when these developmental abilities emerge and change in ways that are relevant to assessment and intervention planning.

Such analyses first require a method to assess the extent to which language and social competence may be validly measured as distinct constructs across a heterogeneous group of very young children with ASD. Using confirmatory factor analysis (CFA), such constructs are represented by latent variables, or factors, that reflect the variance shared between the observed measures (or “indicators”). Since preschoolers with ASD vary considerably with respect to age at diagnosis as well as cognitive and other developmental abilities, and since developmental trajectories in social and language abilities have been shown to differ significantly between individuals, it is important to assess whether the latent variables of interest function in the same manner over time and across different groups of children with ASD. In particular, there may be differences between preschoolers whose difficulties are detected at younger versus older ages due to differences in clinical severity or associated impairment. More specifically, measurement of social competence and language may differ significantly in children depending upon cognitive ability -- for example, it may be more difficult to discriminate between social competence and language in lower-functioning children than in those with higher nonverbal intelligence quotient (IQ).

The goals of this study were threefold: First, we aimed to determine whether social competence and language are distinct developmental constructs in preschoolers with ASD. We compared a two-factor hypothesized model to an alternative one-factor model reflecting one common underlying construct. Social competence and language were measured at three time points (baseline, 6 months and 12 months later), using data from a study involving in a large representative sample of preschoolers aged 2 to 4 years recently diagnosed with ASD. Second, we investigated whether the appropriate latent variable measures were invariant across important clinical groups: children with ASD who were diagnosed at younger versus older preschool ages (as divided by the sample median age), and “complex” children with ASD who also had significant intellectual delay versus more cognitively able children with ASD. Finally, we analyzed whether the discriminant validity – i.e. the social competence and language factors could be measured as distinct constructs – persisted across the different age and IQ subgroups.

METHODS

Sample

The initial sample consisted of 365 newly diagnosed preschool children with ASD participating in a Canadian multisite longitudinal study. Participants met the following inclusion criteria: a) clinical diagnosis of ASD made in the previous four months, confirmed upon enrolment using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000), the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter & LeCouteur, 1994) using Risi's criteria (Risi et al., 2006) and a diagnosis assigned by a study clinician using DSM-IV-TR criteria (American Psychiatric Association, 2000); and (b) chronological age equal to or older than 2 years and younger than or equal to 4 years, 11 months. Exclusion criteria were as follows: (a) cerebral palsy or other neuromotor disorder interfering with study assessments; (b) any known genetic or chromosomal abnormality; or (c) severe visual or hearing impairments. Families were recruited from regional ASD assessment centres in five Canadian cities (Halifax, Montreal, Hamilton, Edmonton and Vancouver). Approval for the study was obtained from Research Ethics Boards at all participating sites. All participating families gave their informed consent.

Children and families were assessed at three time points using a battery of measures at baseline (T1), 6 months later (T2) and 12 months later (T3). For the measures of interest in this study, 345 participants (94.5%) completed T1, 312 (85. 5%) completed T2 and 291 (79.7%) completed T3 assessments. Included among those who did not complete one or more assessments at any time point are thirty-five families (9.6% of entire sample of 365) dropped out of the study after enrolment. Among families still enrolled at T3, 18 did not complete T2 data due to scheduling difficulties or other reasons. There were no differences between study completers and those who dropped out according to child age at diagnosis or ADOS severity score, Vineland total score or language scores at T1.

Procedure

Children were assessed as soon as possible after enrolment in the study. Most children and their primary caregivers completed measures onsite at the academic or hospital centre for ASD assessment in the region, although some children were assessed at home or in their daycare setting to accommodate families. Parents completed semi-structured interviews in person or on the telephone. All interviewers were trained to achieve research-quality levels of expertise. For measures involving interpretation and scoring (ADOS and ADI-R), all interviewers were trained by the same investigator using the same instructional video. Samples of video-recorded assessment sessions and scoring results were checked, with a minimum criterion of 80% inter-rater reliability required prior to conducting actual study assessments.

Measures

The *ADI-R* (Lord, Rutter, & Le Couteur, 1994) is a semi-structured parent interview that assesses developmental milestones and behaviors related to DSM-IV-TR diagnostic criteria for ASD across the domains of socialization, communications and repetitive behaviours and restricted interests (APA, 2000). Items are scored from 0 (no abnormality present) to 3 (extreme abnormality).

The *ADOS* (Lord et al., 2000) is a semi-structured, standardized assessment in which a trained clinician engages participants in activities developed to assess social and communication behaviors indicative of DSM-IV-TR symptoms of ASD.

Preschool Language Scale-4th Edition (PLS-4; Zimmerman, Steiner & Pond, 2002) is an individually administered test used to identify children with language disability. It provides raw scores, standard scores, percentile ranks and age equivalent scores for Total Language (TL), Auditory Comprehension (AC) and Expressive Communication (EC) for children from birth through age 6 years, 11 months, or those who are functioning developmentally in that range. Items designed for preschool children aged 2-4 assess comprehension of basic vocabulary, concepts and grammatical markers (Zimmerman & Castilleja, 2005). The AC subscale evaluates how much a child understands and targets nonverbal skills such as attention to speakers. The EC subscale assesses how well a child communicates with others, and includes assessment of vocal development in infants and toddlers. Test-retest reliability coefficients ranged from .82 to .95 for subscale scores and from .90 to .97 for the Total Language Score (Zimmerman & Castilleja, 2005). Internal consistency coefficients ranged from 0.91-0.94 in children aged 2-4 (Zimmerman, Steiner & Pond, 2002). Scores have been found to be sensitive to change over time, and to differences in language ability in samples of children with ASD (Zimmerman & Castilleja, 2005). Raw scores were utilized to more easily interpret parameters of growth in future longitudinal latent variable modeling.

Research staff continue testing a child until a ceiling is reached according to testing guidelines; should a child continue to progress without reaching a testing ceiling at a given time point (i.e. progress beyond the limits of the PLS-4), then the Clinical Evaluation of Language Fundamentals (CELF) test was also administered at that time point. At the following time point, the child would then only be administered the CELF (n=12 at T2; n=30 at T3). For the purposes of this study, such a child's PLS-4 score would be considered censored (i.e. "missing") at that time point and imputed using multiple imputation procedures outlined below. Therefore, the CELF was not used in the latent variable model, but was included as a predictor in the multiple imputation model.

The Vineland Adaptive Behavior Scales-II (Sparrow, Cicchetti, & Balla, 2005) is a semi-structured interview designed to assess personal and social sufficiency of individuals from birth through to adulthood. It measures strengths and weaknesses in socialization, communication and daily living skills in children aged 0 to 18 years, 11 months old (Mean =100, SD=15). An assessor interviews a respondent most familiar with the child's behavior and rates whether the child performs a given developmental task on a scale from 0-2 ("never" to "usually"). Higher scores demonstrate superior adaptive behavior skills. The Socialization subdomain scales used in this study include: Interpersonal Relationships ("How the child interacts with others", n=38); Play and Leisure Time ("How the individual plays and uses leisure time", n=31); and Social Coping Skills ("How the individual demonstrates responsibility and sensitivity to others", n=30). In this study, interviews were conducted by telephone. Raw scores were used in order to create measurement models that would be easier to interpret in future latent growth curve models.

The Merrill-Palmer-Revised Scales of Development (M-P-R; Roid & Sampers, 2004) is an individually administered measure of intellectual development, appropriate for children aged 2 to 78 months. It was administered at T1 and T3 (only) to reduce response burden for children and parents. In this study, the cognitive domain score was used as a nonverbal indicator of cognitive ability for two purposes: as a predictor in the multiple imputation dataset and as a measure used to divide subgroups based on cognitive ability to assess measurement invariance.

Analyses

Structural equation modeling analyses were carried out using AMOS 17.0 software (Arbuckle, 2006). A CFA approach was used instead of more exploratory techniques such as principal components analysis (PCA) or exploratory factor analysis (EFA), which would be more appropriate for generating hypotheses. In CFA, the number of factors, indicators and covariance estimates are determined a priori, which enables the goodness-of-fit testing of models to underlying patterns in the data. CFA also has the advantage of explicitly modeling measurement error in indicators, as well as the fit of indicators and factors over time.

Patterns of missing data were evaluated (missing at random, missing-not-at-random) and imputed using multiple imputation in SPSS 20.0 statistical software (IBM Corp., 2011) to preserve sample size and to incorporate important variables as predictors of imputed missing values (Graham, 2009). Five datasets substituting imputed for missing values were created and entered separately for analysis in AMOS. One of the unavoidable limitations of the dataset resulted from children “outgrowing” the PLS-4 due to changes in developmental ability over time (i.e., it was not possible to establish a ceiling level of ability on the measure). Therefore, 12 children (3.2%) at T2 and 30 children (8.2%) at T3 were evaluated using the CELF instead of the PLS-4, resulting in non-randomly missing PLS-4 values. Nevertheless, multiple imputation has been described as an appropriate method even when data are not missing at random, provided multiple variables are included in the imputation model (Graham, 2009). Therefore, the following variables were not included in the latent variable measurement model but were used as predictors in the multiple imputation model: child age at diagnosis; child gender (T1); ADI-R social communication score (T1); VABS-II communication standard score

(T1, T2, T3); M-P-R receptive language score, M-P-R developmental index score and CELF core language standard score (T2, T3).

The mean parameter estimates and standard errors for the measurement models across all five imputed datasets were then combined using NORM software for missing data analysis according to standard procedures for MI (Schafer, 1999) Due to significant kurtosis of data, standard errors for parameter estimates were generated using bootstrapping estimation procedures in AMOS to increase their accuracy (Byrne, 2010). Bollen-Stine bootstrapping was also used to adjust for non-normality of distributions in $\chi 2$ analyses (Byrne, 2010). Goodness- of-fit indices (outlined below) were outlined as a range of values, from least to most optimal fit, across all imputed datasets.

Development of Measurement Model (Times 1, 2, 3)

Two latent variables were developed to represent separate social competence and language factors at each time point (T1, T2, T3). The social competence factor represented the shared variance between the VABS socialization domain subscores (interpersonal relationships, play and leisure, social coping). The language latent variable represented the variance shared between the auditory comprehension (PLS-AC) and expressive communication (PLS-EC) scores of the PLS-4. Latent variables were estimated to measure a given construct well if each indicator contributed a significant amount of variance to the construct, as demonstrated by a minimally acceptable standardized factor loading (B = 0.4, $p < 0.01$), and if the fit of the latent variable to the underlying data met generally agreed-upon criteria of adequate goodness-of-fit (Tucker-Lewis Index [TLI] ≥ 0.90; Comparative Fit Index [CFI] ≥ 0.95; Root Mean Square Error of Approximation [RMSEA] ≤ 0.10) (Browne & Cudeck, 1993; Hu & Bentler, 1999; MacCallum et al., 1996). The chi-squared test of fit was also described, but not included as a criterion of fit, as it has been described as overly stringent and too likely to reject well-fitting models in the presence of larger sample sizes (MacCallum et al., 1996).

Assessment of Temporal Invariance.

This form of measurement invariance determines whether the latent variable representing the construct of interest functions in the same way from one time point to the next in longitudinal studies. Factorial equivalence testing was conducted including all three time points simultaneously. Factor loadings for the same indicators at each time point were constrained to equal each other; a significant change of fit in both the chi-squared and CFI estimates ($\Delta\chi 2$, $p < 0.05$; ΔCFI > 0.01) when compared to the baseline unrestricted model would indicate a lack of measurement invariance.

Assessment of Multi-Group Measurement Invariance (Times 1, 2, 3)

Multi-group invariance assesses whether the form and function of the latent variables are equivalent between specific groups of interest where there is reason to consider that they may function differently. For example, children who are diagnosed at a younger age may differ significantly from older children because of important characteristics, e.g., more severe symptoms or impairment leading to earlier detection. Further, children who are cognitively lower-functioning may demonstrate different patterns of language development, for example revealing different associations between receptive and expressive abilities compared to more cognitively advanced children. Invariance of form implies that the same number of factors and indicators applies to both groups. Invariance of factor loadings shows that a unit change in the underlying construct represented by the latent variable (e.g., social competence) is associated with statistically equivalent change in the indicators in both groups (Brown, 2006, p.282). More stringent tests of invariance were not pursued, because non-invariance of form and factor loadings are considered to be sufficiently strict for most longitudinal SEM analyses (Brown, 2006, p257; Byrne, 2010).

The test of invariance of form evaluates the goodness-of-fit of individual Social Competence and Language latent variables separately in each group. Children were divided into two sets of comparison subgroups: younger and older groups using the median age at diagnosis

(37.5 months), lower- vs. higher-scoring on cognitive tests, using a cut-off of 70 standard score (SS) points on the baseline Merrill-Palmer-Revised Cognitive Domain (MPR-CD) score. In the second step, factor loadings for the same indicators (e.g., VABS interpersonal relationships score at T1, T2, T3) were constrained to equal each other across groups; a statistically significant degradation of fit ($\Delta\chi 2$, $p < 0.05$; Δ CFI > 0.01) compared to the unconstrained model would indicate significant variance in factor loadings between groups (Byrne, 2010).

RESULTS

The sample comprised 305 boys and 65 girls, with a mean age at diagnosis of 38.21(8.48) months. The mean cognitive standard score on the M-P-R was 57.29(24.65), indicating mild-moderate intellectual disability in the group on average. The mean standardized Socialization score on the VABS-II was 72.24(9.02), and the mean Auditory Comprehension and Expression Communication subscores on the PLS-4 were 65.12(19.89) and 69.78(17.30), respectively. The sample mean on the ADOS severity metric was 7.67(1.65).The children younger than the median age of 37.5 months at diagnosis had significantly lower M-P-R cognitive scores at T1 compared to the older group but did not differ on ADOS indices of ASD symptoms. Children with cognitive scores below 70 SS points had significantly lower VABS-II Socialization standard scores compared to those with scores over 70 (See Table 1). . Tables 2a and 2b present the means; standard deviations and ranges for the VABS subdomain standard and raw scores and the PLS-4 Auditory Comprehension and Expressive Communication standard and raw scores. The children in the sample demonstrated notable growth in social skills, and particularly in language abilities over the course of the first year after diagnosis. On average, the group's standard score increased by over 8 points on the AC score of the PLS-4. Examination of subgroups revealed apparent differences, particularly on the language measures, where children with higher cognitive scores appeared to develop more quickly. (See Supplementary Tables 1A and 1B).

Measurement Model

Social Competence Factor

Factor loadings for all indicators across all time points were statistically significant. The Interpersonal Relationships indicator consistently loaded most strongly across all time points (standardized Beta = 0.87 to 0.90), contributing the greatest amount of variance. Social Coping loading most weakly (standardized Beta = 0.60 to 0.74, $p < 0.01$). Correlations between latent variables ranged from 0.70 (T1-T3) to 0.83 (T2-T3). Fit was excellent across all imputed datasets (see Table 3).

Emerging Language Factor

Examination of the factor loadings for the AC and EC subscales of the PLS-4 indicated considerable collinearity, with standardized factor loadings greater than 0.90 ($p<0.01$) at each time point. Correlations between time points were very high, ranging from 0.88 ($p<0.01$; T1 to T3) to 0.93 ($p<0.01$; T1 to T2). Fit indices ranged from excellent to mediocre: CFI and TLI values were consistently above 0.95 across all datasets, while RMSEA values ranged from 0.1 to 0.14. Inadmissible solutions were achieved in two out of five imputed models, with messages indicating “non-positive-definite” matrices. The measurement model for emerging language therefore indicated that the Auditory Comprehension and the Expressive Communication subscales essentially measured the same construct, and that a latent variable was not necessary — either observed score could be used to represent the construct of emerging language. Nevertheless, measurement invariance testing was performed to determine if this held true in younger as well as older preschoolers, and in individuals with lower- and higher IQs, because the relation between expressive and receptive language may vary according to age and ability (see Table 4.)

The fit for a two-factor model was excellent, and significantly better than for the one-factor model. The hypothesized two-factor model demonstrated excellent fit to the data at each time point ($\chi 2=2.10$ (4, $p=0.70$) to 8.17(5, $p=0.09$); TLI=0.99-1.0; CFI=1.0; RMSEA = 0.01 to 0.05). Examination of a one-factor, five-indicator model comprising VABS social competence and PLS-4 language indicators demonstrated very poor fit to the underlying data at each time point ($\chi2$=171.06 [5df], $p < 0.01$) to 182.51 ([5df], $p < 0.01$); TLI =0.73 -0.76, CFI=0.87-0.88;RMSEA = 0.3-0.32). Pooled factor loadings demonstrated very high standardized loadings for language indicators (β=0.95, $p < 0.01$) and moderate factor loading strengths for the VABS indicators ranging from β= 0.58 to β=0.70 ($p<0.01$). The 1-factor, 2-factor models were also assessed in the younger versus older and lower- versus higher-IQ groups as described above, yielding the same pattern of results. Across all subgroups of interest, the 2-factor model represented a significantly improved fit over the 1-factor model.

Measurement Invariance

Social Competence Factor

There was no significant change in fit between the temporal invariance model, which constrained the factor loadings of respective VABS Social subdomains across time points, and the baseline model ($\Delta\chi2$ [3df] ranged from 1.05, p=0.90 to 3.63, p=0.47; ΔCFI =0.00 to 0.001). Therefore, the latent variable functioned in the same manner across time points. Invariance was then assessed between groups comprising younger and older preschoolers (median age of 37.5 months) and lower- versus higher- than 70 SS points on M-P-R cognitive score. Fit was excellent in both younger and older groups across all imputed datasets

(TLI and CFI > 0.95; RMSEA < 0.08). Factor loadings were also equivalent between groups ($\Delta\chi 2$[6df] ranging from 2.88 to 4.97, p>0.1 and ΔCFI =0.00 to 0.002 across all datasets). Invariance of form and factor loadings was also confirmed for groups below and above a cognitive score of 70 SS points ($\Delta\chi 2$[6df] ranging from 3.9 to 9.58, p>0.10 and ΔCFI =0.001 to 0.002) (*s*ee Supplementary Tables 2A and 2B).

Language Factor

Testing of temporal invariance revealed a significant chi-squared change of fit across all imputed datasets ($\Delta\chi 2$[2df] = 18.33, p<0.01 to 27.23, p<0.01) but the change in CFI was less than 0.01 across all datasets. Furthermore, standardized factor loadings for the AC and EC subscales onto the latent factor were over 0.95 across all time points. Therefore, while there may have been slight differences in how the subscales relate to the latent variable at each time point, they were remained highly correlated that at all time points either subscale could be used. The same results were found in assessing multi-group invariance. The fit of the language factor measured across T1-T2-T3 was excellent according to CFI and TLI in both younger and older groups (>0.95 across all datasets for both groups). However, the RMSEA ranged from 0.00 (good fit) to 0.12 (poor fit) in the both comparison groups across all datasets, likely reflecting the high collinearity in the factor indicators (see

Supplementary Tables 3A and 3B). Standardized factor loadings were greater than 0.84 for all subscales across all time points in both groups. Constraining the factor loadings to equivalence between groups led to non-significant changes in fit according to the chi-squared difference test in 4/5 datasets ($\Delta\chi 2$[3df] = 3.17, p=0.37 to 8.90(3), 0.03; CFI change 0.00-0.001).

A comparison of lower- versus higher- IQ groups also revealed a similar pattern. The fit was excellent in both groups across all datasets according to the CFI and TLI (0.96-1.0). However, the RMSEA was borderline or unacceptable (0.08-0.14) in both groups. Again, factor loadings for both subscales across all time points were high in both groups (ß=0.84-0.97), indicating high collinearity. Testing of factorial invariance yielded a significant degradation in fit on chi-squared difference tests in 4/5 datasets ($\Delta\chi 2$ [3df] = 2.66, p=0.45 to 15.45, $p<0.01$) but insignificant deterioration of fit according to CFI test of difference (ΔCFI = 0.001-0.005). Tests of partial invariance identified T2 as a time point when the EC subscale loaded somewhat differently. However, because both subscales loaded so highly across all time points in both cognitive-ability groups and because of the insignificant deterioration in CFI fit the language factor could be considered invariant across these groups. Thus, measurement invariance tests indicated that the subscales measuring receptive and expressive language on the PLS-4 functioned in relatively the same manner in younger and older and in lower and higher-IQ preschoolers with ASD. However, the very high factor loadings of the subscales onto the latent variable indicated that the observed score of either variable adequately captured the variance shared between them and therefore should be used, rather than a latent variable representation to improve stability of the model.

DISCUSSION

Results indicate that the social subdomains of the Vineland Adaptive Behavior Scale and the Preschool Language Scale-4 are distinct measures of the constructs of emerging social competence and language ability in preschoolers newly diagnosed with ASD. This finding is in stark contrast with other measurement models of ASD suggesting that social and communication abilities comprise one construct (Boomsma, et al., 2008; Frazier, et al., 2008; Georgiades, et al., 2007; Gotham, et al., 2007; Snow, et al., 2009; Van Lang, et al., 2006). These earlier studies were intended to clarify the ASD phenotype and used measures of communication in children with ASD, emphasizing more pragmatic elements of language rather than the more structural aspects such as syntax and vocabulary that are emphasized in the PLS-4.

Subgroup analysis found the constructs to be more highly correlated in preschoolers who were older than the median age of 37.5

months and who were above 70 SS points on the MPR Cognitive Score IQ. This finding was somewhat surprising because one might expect more overlap in social and language scales early on, as both measure shared skills such as joint attention – the ability to attune one's focus to object or event of shared interest with another person. This finding may reflect the reciprocal nature of social competence and structural language that builds over time. For example, children with greater cognitive abilities also had higher baseline social competence with ASD; having greater joint attention skills (e.g. pointing, gaze following) could lead to greater receptive vocabulary learning, which in turn leads to improved social communication and capacity to use language to better decode interpersonal situations.

In spite of remarkable change over time, and differences in developmental abilities between subgroups divided by median age and nonverbal IQ, the overall fit and factor loadings of the social competence latent variable in this study did not vary over time or between groups. This indicates that the measure functions in a similar way across these factors/variables in this sample. This was important to assess because the relevance of the adaptive behaviors assessed by the individual subscales of the Vineland social domain differs somewhat by age and ability. For example, the Interpersonal Relationships domain assesses a greater number of earlier-emerging skills such as looking at faces and showing a preference for certain people, while the Social Coping domain asks questions about behaviors such as transitioning between activities and controlling impulses, which may be more relevant to somewhat older or more developmentally advanced preschoolers. Tests of measurement invariance revealed that such issues were minimal in this sample of young children with ASD.

The language measure also appeared to be invariant over time and between groups. However, the development of an emerging language measurement model using the Auditory Comprehension and Expressive Communication subscores of the PLS-4 revealed high collinearity of both indicators across all time points, suggesting that either observed score could serve as a proxy measure of the construct of emerging language as measured by the latent variable. This is particularly relevant because children with ASD, as a group, may demonstrate a discrepancy between receptive and expressive language that differ quite markedly from typically developing children yet vary significantly between individuals (Volden et al. 2010). Characterizing a child's unique developmental profile of abilities across language domains in young children with ASD may be very useful for prognosis and intervention planning. For example, Anderson et al. (2009) found that receptive versus expressive deficits may be differentially predictive of higher versus lower adaptive functioning trajectories. The results of this study emphasize that any such findings may depend on the particular measures used: more specifically, the PLS-4 subscales may not be sensitive enough to detect different developmental trajectories across these two language domains in young preschoolers with ASD.

To our knowledge, this is the first study to develop latent variable measurement models of social competence and language over multiple time points in a sample of preschoolers with ASD. The findings lay important measurement groundwork for longitudinal modeling of key developmental abilities in ASD. More specifically, they confirm that the Vineland Adaptive Behavior Scales (social subdomains) and the PLS-4 demonstrate excellent properties for use in longitudinal latent variable modeling in a sample of young children with ASD. Although the children as grouped in these analyses differed significantly with respect to age at diagnosis and cognitive ability, the measures functioned in approximately the same manner, which provides reassurance of their usefulness in such a population. Furthermore, because both early social competence and language are important abilities in their own right, as well as important predictors of the later development of other abilities such as adaptive functioning across a variety of domains (Anderson, et al., 2007; Anderson, et al., 2009; Bennett et al., 2008) and also later symptom burden (Bennett, et al., 2008), it is important to determine whether they can be distinctly measured early on in children's developmental trajectories.

Several limitations in this study must nevertheless be noted. First, a proportion of children who had higher language abilities lacked PLS-4 scores for nonrandom reasons — that is they surpassed the ceiling limits of that test and were therefore given a different language test (the CELF). This is a common problem in developmental research but it is unlikely to have affected the overall results because of the relatively small amount of non-randomly missing data (less than ten percent), and because multiple imputation was used, taking CELF scores into account scores as well as multiple other measures of language. Second, ideally multiple measures of social competence and language ability, using multiple informants, would have been used to develop each latent variable, capitalizing on one of the strengths of confirmatory factor analysis techniques. However, appropriate measures were not available within this dataset across all time points. Third, due to limitations in the dataset, which comprised only subscale scores, CFA at the item level was not possible. Future studies using more fine-grained item-level analysis, such as Item Response Theory (IRT) may be able to determine more specifically whether certain questions are more or less able to discriminate between receptive and expressive language in subgroups of preschoolers with ASD. Finally, the relatively short timeframe of this study limits generalizability of the results to older groups or over longer periods of time. Follow-up studies should attempt to include multiple measures and informants, thereby extending findings into older age groups.

Meanwhile, these results confirm that the Vineland Adaptive Behavior Scales and the Preschool Language Scales are able to measure social competence and language abilities as distinct constructs when they emerge during this key period of development in young children with ASD despite evidence of moderate to strong associations between them. Language may therefore be measured as a separable, and very important, component of the ASD phenotype even in very young children, with an aim to assess delays or deficits early on for targeted speech-language therapy if needed. Furthermore, children who are older or who are more developmentally advanced at time of diagnosis may demonstrate stronger associations between social competence and language domains, which may be the result of different, more dynamic cross-domain learning cascades. Future research should focus on the nature of interactive trajectories and whether they differ between important subgroups of very young children with ASD. Variation and change in these abilities demonstrated by very young children with ASD underscore that ASD is a disorder of multiple important phenotypes, not just social communication and repetitive and stereotyped behaviors. An appropriate assessment of any child where ASD is a possibility should therefore take a multiple phenotype approach, in addition to confirming the diagnosis, to optimize the tailoring of interventions and the monitoring of development over time.

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Table 1. Sample Characteristics, Divided by Subgroups.

	ADOS Severity Score	**M-P-R Cognitive Score SS**	**Child Age at Diagnosis (mo.)**	**VABS Social Standard Score**
Younger – vs. Older- Age at Diagnosis				
Younger (<37.5 mo.), n=183	7.58(1.69)	52.87(19.58)	31.39(3.88)	73.11(8.81)
Older (37.5 + mo.), n=182	7.77(1.61)	61.88(28.33)**	45.29(5.68)**	71.33(9.16)
Lower vs. Higher Cognitive Scores on M-P-R CS*				
Less cognitively able (<70 SS)*, n=265	7.63(1.67)	44.57(14.90)	37.06(7.60)	70.34(8.34)
More cognitively able (70+ SS)*, n=100	7.43(1.59)	88.58(17.08)**	41.48(9.61)**	77.31(8.82)**

*M-P-R CS = Merrill-Palmer Revised Cognitive Domain Score

** Significant difference of means (independent samples T-test) between subgroups of interest: age-at-diagnosis (i.e. younger vs. older) and cognitive-ability groups (i.e. lower vs. higher cognitive scores), $p < 0.01$

Table 2a. Mean Raw Scores/Standard Scores on VABS-II Socialization Subdomains (Standard Deviation)

T1 IR	T1 PLT	T1 SC	T2IR	T2PLT	T2 SC	T3 IR	T3 PLT	T3 SC
24.82(7.62) 9.32(1.91)	14.29(8.05) 9.95(2.08)	7.40(4.51) 10.93(1.77)	30.04(9.83) 9.95(2.48)	19.89(10.33) 10.59(2.64)	9.47(5.69) 10.69(2.07)	33.18 (10.60) 10.21(2.57)	23.62(11.13) 10.80(2.82)	11.30 (6.33) 10.74 (2.04)

Vineland Adaptive Behavior Scales-II Subscales: IR = Interpersonal Relationships; PLT=Play and Leisure Time; SC= Social Coping

Table 2b. Mean Raw Scores/Standardized Scores on Preschool Language-Test-4 (PLS-4) Subscales

T1 AC	**T1EC**	**T2 AC**	**T2 EC**	**T3 AC**	**T3 EC**
26.82(11.59) 65.09(19.93)	29.11(10.94) 69.70(17.03)	32.14(13.36) 69.93(22.54)	34.24(13.57) 72.12(20.08)	37.50(14.19) 73.88(22.98)	38.94(14.23) 73.09(22.12)

AC = Auditory Comprehension; EC = Expressive Communication

TABLE 3. Measurement Model, Social Competence (Vineland Adaptive Behavior Scales-II) at Times 1, 2 and 3.

	Parameter Estimate	Standard Error	Standardized Parameter Estimate	p-value
Factor Loadings (B)				
T1 Interpersonal Relationships	1.00	---	0.88	P < 0.01
T1 Play and Leisure Time	0.97	0.06	0.81	P < 0.01
T1 Social Coping	0.47	0.03	0.70	P < 0.01
T2 Interpersonal Relationships	1.00	-----	0.91	P < 0.01
T2 Play and Leisure Time	0.97	0.05	0.83	P < 0.01
T2 Social Coping	0.43	0.03	0.68	P < 0.01
T3 Interpersonal Relationships	1.00	-----	0.90	P < 0.01
T3 Play and Leisure Time	0.96	0.05	0.86	P < 0.01
T3 Social Coping	0.43	0.03	0.72	P < 0.01
Variance				
T1 Social Competence	2.77	0.32	---	P < 0.01

T2 Social Competence	4.42	0.55	----	P < 0.01
T3 Social Competence	5.03	0.50	----	P < 0.01
Covariance Between Latent Variables	**Covariance**	**SE**	**Correlation (r)**	**p-value**
T1-T2	44.73	4.50	0.74	P < 0.01
T2-T3	75.12	5.48	0.84	P < 0.01
T1-T3	49.17	4.71	072	P < 0.01
Goodness of Fit of Measurement Model T1-T3	**χ2, 15 df**	**TLI**	**CFI**	**RMSEA**
Imputation #1	28.82; p=0.06	0.99	1.00	0.04
Imputation #2	28.69; p = 0.05	0.99	1.00	0.04
Imputation #3	30.15; p =0.04	0.99	0.99	0.04
Imputation #4	35.70; p = 0.01	0.98	0.99	0.05
Imputation #5	26.65; p=0.09	0.99	1.0	0.04

TABLE 4. Measurement Model, Language Ability (Preschool Language Scale-4)

	Parameter Estimate	**Standard Error**	**Standardized Parameter Estimate**	**p-value**
Factor Loadings (B)				
T1 Auditory Comprehension	1.0	----	0.92	---
T1 Expressive Communication	0.87	0.03	0.93	0.001
T2 Auditory Comprehension	1.00	----	0.95	-----
T2 Expressive Communication	0.87	0.02	0.94	0.001
T3 Auditory Comprehension	1.00	-----	0.87	-----
T3 Expressive Communication	1.02	0.02	1.00	0.001
Variance				
T1 Language Ability	334.49	29.63		0.001
T2 Language Ability	477.15	39.10		0.001
T3 Language Ability	528.50	46.49		0.001
Covariance (correlation)				
T1-T2 Language Ability	372.61	30.98	0.93	0.001
T2-T3 Language Ability	454.84	39.26	0.91	0.001
T1-T3 Language Ability	370.43	32.25	0.88	0.001

Goodness of Fit of Measurement Model T1-T3	**χ2, 3 df**	**CFI**	**TLI**	**RMSEA**
#1	25.43, p<0.001	0.99	0.96	0.14
#2	16.83, p=0.001	1.0	0.98	0.11
#3	20.05, p<0.001	0.99	0.97	0.13
#4	13.40; p<0.004	1.0	0.98	1.0
#5	16.85, p=0.01	1.0	0.98	0.11

Supplementary Tables

TABLE 1A: Vineland Social Subdomain Scores, Raw and Standardized, by Subgroup

GROUP	T1 IR	T1 PLT	T1 SC	T2IR	T2PLT	T2 SC	T3 IR	T3 PLT	T3 SC
Participants Diagnosed at Younger(< 37.5 mo.) vs. Older (37.5 mo. +) Ages									
Younger (<37.5 mo.)	21.91 (5.96) 9.44 (1.75)	11.14 (6.25) 10.11 (2.07)	5.72 (3.46) 11.37 (1.76)	26.66 (8.71) 9.86 (2.54)	16.26 (8.73) 10.65 (2.61)	8.09 (5.40) 11.15 (2.11)	30.02 (8.96) 10.05 (2.42)	20.06 (9.87) 10.72 (2.74)	9.72 (5.03) 10.91 (1.90)
Older (37.5+ mo.)	27.05 (8.13)* 9.23 (2.05)	16.68 (8.57)* 9.83 (2.10)	8.67 (4.83)* 10.58 (1.72)*	32.83 (9.94)* 10.10 (2.46)	22.54 (11.01)* 10.52 (2.84)	10.66 (5.92)* 10.43 (2.08)	36.62 (11.04)* 10.52 (2.65)	26.70 (11.35)* 10.93 (3.02)	12.89 (6.35)* 10.69 (1.98)
Participants with Lower- (< 70 SS points) vs. Higher (≥ 70 SS points) on Merrill-Palmer Cognitive Domain Score									
Lower Cog Score (<70 SS)	22.68 (6.52) 8.88 (1.76)	12.24 (6.54) 9.57 (1.85)	6.44 (3.71) 10.74 (1.72)	27.59 (8.64) 9.45 (2.29)	17.19 (9.13) 10.01 (2.46)	8.43 (5.21) 10.49 (2.03)	31.06 (10.05) 9.76 (2.44)	21.06 (10.30) 10.20 (5.31)	10.18 (1.83) 10.46 (1.83)
Higher Cog Score (70+ SS)	30.56 (7.66)* 10.49 (1.85)*	19.73 (9.41)* 10.97 (2.36)*	9.92 (5.42)* 11.42 (1.88)*	37.03 (8.91)* 11.46 (2.18)*	26.84 (10.00)* 12.11 (2.59)*	12.53 (6.22)* 11.42 (2.22)*	40.46 (8.64)* 11.78 (2.13)*	31.19 (9.53)* 12.53 (6.27)*	15.09 (1.92)* 11.65 (1.92)*

* Means significantly different between comparison groups (independent samples T-test; $p<0.01$)

TABLE 1B: PLS-4 Subdomain Scores, Raw and Standardized by Comparison Subgroups

GROUP	T1 AC	T1EC	T2 AC	T2EC	T3 AC	T3 EC
Participants Younger- (< 37.5 months) vs. Older (≥37.5 months) Age of Diagnosis						
Younger (<37.5 mo.)	21.30(6.69) 60.56(15.81)	23.71(7.09) 67.91(14.01)	26.53(9.70) 65.83(20.41)	28.82(8.94) 71.52(16.43)	32.82(12.12) 72.54(24.03)	33.94(11.22) 72.10 (19.86)
Older (37.5+ mo.)	30.99(12.91)* 68.60(22.20)*	33.28(11.94)* 71.20(19.23)*	36.62(13.69)* 73.41(22.26)*	38.57(13.22)* 72.95(20.49)*	41.66(13.30)* 75.96(20.06)*	43.03(13.12)* 72.46(19.86)
Participants with Lower- (< 70 SS points) vs. Higher (≥ 70 SS points) on Merrill-Palmer Cognitive Domain Score						
Lower Cog Score (<70 SS)	22.09(7.26) 56.59(11.32)	24.92(7.17) 63.10(10.88)	26.85(9.93) 60.60(15.53)	29.22(9.17) 64.39(13.32)	32.30(11.69) 65.23(18.71)	33.23(10.46) 64.26(15.46)
Higher Cog Score (70+ SS)	39.37(11.19)* 87.91(20.00)*	40.41(11.10)* 87.63(17.58)*	46.69(9.89)* 95.60(18.11)*	48.06(10.25)* 93.55(17.78)*	52.60(8.30)* 99.20(17.11)*	54.18(8.93)* 97.37(15.98)*

* Means significantly different between comparison groups (independent samples T-test; $p<0.01$)

TABLE 2A: Measurement Invariance, Invariance of Form, Social Competence by Age-at-Diagnosis Subgroups

Imputed Dataset	$\chi 2$, 18 df	CFI	TLI	RMSEA
Participants < 37.5 months old at time of diagnosis				
#1	25.96, p=0.1	0.99	0.98	0.05
#2	25.41, p=0.11	0.99	0.98	0.05
#3	26.95, p=0.08	0.99	0.97	0.05
#4	16.00, p=0.59	1.0	1.0	0.00
#5	24.37,p=0.14	1.0	1.0	0.04
Participants ≥37.5 months old at time of diagnosis				
#1	25,45, p=0.11	0.99	0.99	0.05
#2	20.19, p=0.32	1.0	1.0	0.03
#3	30.22, p=0.04	0.99	0.98	0.06
#4	38.46, p=0.03	0.98	0.96	0.08
#5	21.46, p=0.26	0.99	0.99	0.03

TABLE 2B: Measurement Invariance, Factorial Invariance, Social Competence, Younger vs. Older Age at Diagnosis

Imputed Dataset	**$\Delta\chi 2$, 6 df**	**Change CFI**
#1	4.08 p=0.67	0.001
#2	3.59, p=0.73	0.001
#3	4.97,p=0.55	+0.001
#4	2.88, p=0.82	0.002
#5	3.41, p=0.76	+0.001

TABLE 2C: Measurement Invariance, Invariance of Form, Social Competence, Lower vs. Higher Cognitive Score Subgroups

Imputed Dataset	$\chi 2$, 18 df	CFI	TLI	RMSEA
Participants < 70 SS points on MPR-CS				
#1	23.23, p=0.18	1.0	0.99	0.03
#2	19.94, p=0.34	1.0	1.0	0.02
#3	17.33, p=0.50	1.0	1.0	0.00
#4	22.60, p=0.21	1.0	0.99	0.03
#5	25.98, p=0.10	0.99	0.99	0.04
Participants ≥ 70 SS points on MPR-CS				
#1	25,45, p=0.11	0.99	0.99	0.05
#2	20.19, p=0.32	1.0	1.0	0.03
#3	30.22, p=0.04	0.99	0.98	0.06
#4	38.46, p=0.03	0.98	0.96	0.08
#5	21.46, p=0.26	0.99	0.99	0.03

TABLE 2D: Measurement Invariance, Factorial Invariance, Social Competence, Lower vs. Higher Cognitive Score Subgroups

Imputed Dataset	**$\Delta\chi 2$, 6 df**	**Change CFI**
#1	3.98 p=0.68	0.001
#2	6.39, p=0.91	0.000
#3	6.54,p=0.37	0.000
#4	4.88, p=0.56	0.000
#5	9.58, p=0.14	0.002

TABLE 3A: Measurement Invariance, Invariance of Form, Language Ability, Younger- vs. Older Age at Diagnosis Subgroup

Imputed Dataset	$\chi 2$, 1 df	CFI	TLI	RMSEA
Participants < 37.5 months old at time of diagnosis				
#1	3.5, p=0.06	1.0	0.97	0.12
#2	0.04, p=0.95	1.0	1.0	0.00
#3	0.17, p=0.68	1.0	1.0	0.00
#4	0.66, p=0.42	1.0	1.0	0.00
#5	0.02, p=0.96	1.0	1.0	0.00
Participants ≥37.5 months old at time of diagnosis				
#1	1.32, p=0.25	1.0	1.0	0.04
#2	0.002, p=0.97	1.0	1.0	0.00
#3	2.31, p=0.13	1.0	0.99	0.09
#4	0.001, p=0.98	1.0	1.0	0.00
#5	0.67, p=0.42	1.0	1.0	0.00

TABLE 3B: Measurement Invariance, Factorial Invariance, Language Ability, Younger- vs. Older Age at Diagnosis

Imputed Dataset	**$\Delta\chi 2$, 3 df**	**Change CFI**
#1	8.90 p=0.03	0.002
#2	3.17, p=0.37	0.000
#3	4.40,p=0.22	0.000
#4	4.94, p=0.13	0.001
#5	8.05, p=0.05	0.001

TABLE 3C: Measurement Invariance, Invariance of Form, Language Ability, Lower vs. Higher Cognitive Score Subgroups

Imputed Dataset	**χ2, 1 df**	**CFI**	**TLI**	**RMSEA**
Participants < 37.5 months old at time of diagnosis				
#1	12.73, p<0.01	0.99	0.96	0.11
#2	10.13, p=0.02	0.99	0.97	0.07
#3	13.93, p<0.01	0.99	0.96	0.12
#4	13.54, p<0.01	0.99	0.96	0.12
#5	10.27, p=0.02	0.99	0.97	0.10
Participants ≥37.5 months old at time of diagnosis				
#1	5.01, p=0.17	1.0	0.98	0.08
#2	6.15, p=0.11	0.99	0.97	0.11
#3	2.61, p=0.46	1.0	1.0	0.00
#4	9.77, p=0.02	0.99	0.94	0.15
#5	7.81, p=0.05	0.99	0.96	0.13

TABLE 3D: Measurement Invariance, Factorial Invariance, Language Ability, Lower- vs. Higher Cognitive Score Subgroups

Imputed Dataset	**$\Delta\chi 2$, 3 df**	**Change CFI**
#1	10.34, p=0.02	0.003
#2	7.90, p=0.05	0.002
#3	8.48,p=0.04	0.003
#4	2.66, p=0.45	0.001
#5	15.45, p=0.01	0.005

CHAPTER 3

STUDY 2

TITLE: Do Reciprocal Associations Exist Between Social and Language Pathways in ASD?

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CONTEXT AND IMPLICATIONS: The second paper of this ‘sandwich thesis’ builds upon the measurement model developed in the first to test a model of ‘reciprocal cascade effects’ between the domains of social competence and language ability in preschool-aged children with ASD. Results indicate that these abilities do not appear to build off each other in a reciprocal manner in the first year after diagnosis but instead appear to become more specialized and stable over time. This pattern resembles that observed in typical development. Furthermore, certain baseline differences were observed between children with “normal-range” versus impaired cognitive abilities, however the overall pattern of dissociation between domains did not differ between groups.

This study is the largest of its kind to test interactions between social and language domains in very young children with ASD during the first year after diagnosis, and the first to test for reciprocal patterns of development. It spans a very sensitive period for the emergence of these skills and provides important insights for the delivery of optimal early intervention.

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Abstract

Differences in how developmental pathways interact dynamically in children with ASD likely contribute in important ways to phenotypic heterogeneity. **Objectives:** This study aimed to model longitudinal reciprocal associations between social competence (SOC) and language (LANG) pathways in young children with ASD. **Methods:** Data were obtained from 365 participants aged 2-4 who had recently been diagnosed with an ASD and who were followed over 3 time points: baseline (time of diagnosis), 6- and 12 months later. Using structural equation modeling, a cross-lagged reciprocal effects model was developed that incorporated auto-regressive (stability) paths for SOC (using the social subscales of the Vineland Adaptive Behavior Scale-II) and LANG (auditory comprehensive subscale of the Preschool Language Scale-4). Cross-domain associations included within-time correlations and lagged associations. **Results:** Domains were highly stable, with strong within-domain associations from one time point to the next. Significant but small reciprocal cross-lag associations were found across most time points and within-time correlations decreased over time. **Conclusion**: Longitudinal reciprocal cross-domain associations between social competence and language were very small in this sample of young children with ASD. Instead, a pattern emerged to suggest that social competence and language ability were fairly strongly associated around time of diagnosis in

preschoolers with ASD, then diverge and appear to become more specialized rather than interdependent over the ensuing 12 months.

INTRODUCTION

Children with autism spectrum disorders (ASDs) typically demonstrate common core differences in social reciprocity and communication abilities as well as repetitive, restricted or stereotyped behaviours. However, there is substantial heterogeneity of symptoms, related impairment and functioning across individuals with such diagnoses. ASDs may therefore be best understood as disorders with multiple phenotypes. In order to link common early impairment or differences (e.g. at the level of genes or brain structure and function) to later variability across a range of autistic symptoms, co-morbidity and daily functioning, we need to better understand the complex developmental processes that occur in between (Dawson et al., 2002; Karmiloff-Smith, 1998; Mundy, Henderson, Inge, & Coman, 2007; Tager-Flusberg, 2010).

Early social and language developmental pathways, and the interactions between these, are important candidate processes linking early impairment or differences and later heterogeneity of phenotypes in individuals with ASD. According to Social Orientation Theory (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998) and similar social-developmental theories of ASD, critical levels of impairment in emerging social competence (e.g. orienting to faces, engagement in joint attention, imitation) likely play an important role in the underlying pathophysiology of ASD (Charman, 2003; Dawson, et al., 2002; Mundy, Sullivan, &

Mastergeorge, 2009; Mundy, et al., 2007). Yet between individuals across this spectrum of diagnoses there appears to be significant variability in the extent of such social-developmental deficits (e.g. joint attention, looking at faces, responding to infant-directed speech) (Charman et al., 2003; Dawson, et al., 1998; Mundy, Gwaltney & Henderson, 2010; Parish-Morris, Hennon, Hirsh-Pasek, Golinkoff, & Tager-Flusberg, 2007). This variation in degree of impairment in upstream causal factors could spread across the development of multiple other domains downstream, beginning with language skills (Dawson, et al., 1998; Dawson et al., 2005).

Such patterns have been described as developmental cascades – when early advantages or constraints in specific skills or developmental processes influence the trajectories of other domains, leading to a spreading of effects across multiple pathways over time in feedback or feed-forward patterns (Masten & Cicchetti, 2010). Variation in the degree of impairment in critical upstream processes such as emerging social competence may lead to different developmental cascade patterns of association with other unfolding developmental abilities (e.g. language, self-regulation), in turn leading to greater heterogeneity in core ASD symptoms and important co-morbidities, e.g. intellectual disability, language impairment or anxiety problems (Dawson, et al., 2002; Mundy, et al., 2007). In keeping with such theories, several promising interventions aim to optimize emerging social skills and their subsequent developmental spillover effects (Dawson et al., 2010; Kasari, Gulsrud, Wong, Kwon, & Locke, 2010). Understanding whether and how developmental cascades may occur, and how they may differ between children with ASD and differing symptom or co-morbidity profiles, may illuminate our understanding of developmental contributions to the heterogeneity of the ASD phenotype. This in turn would help to tailor ASD interventions in more developmentally sensitive ways.

A review of the cognitive-developmental and longitudinal research that has examined associations between social and language development in ASD suggests that the two domains may be reciprocally related over time. Early advantages in social skills may either reflect greater social motivation or interest, leading to more proficient language learning either directly (i.e. pointing at and naming objects, listening to stories) or indirectly (i.e. watching others interact) (Charman, 2003; Dawson, et al., 1998; Mundy, Sigman, & Kasari, 1990; Parish-Morris, et al., 2007). Enhanced language abilities, meanwhile, have been associated with higher scores on theory of mind tasks (Bennett et al., 2013; Hale & Tager-Flusberg, 2003) and enhanced play skills (Tager-Flusberg & Caronna, 2007), and may benefit social development as more linguistically competent children use their verbal skills to reason through social scenarios (Fisher, Happe, & Dunn, 2005). In this manner, different skill pathways may interact and build off each other within the context of each child's development and experience of his/her environmental contexts in a reciprocally cascading pattern. Even relatively small early advantages in some children with ASD as compared to others may become amplified through reciprocal feedback loops: For example, relatively small advantages in early joint attention or social reciprocity may lead to comparatively better vocabulary, which may then scaffold a child's theory of mind development or offer greater opportunity for social learning, thus in turn feeding back to enhance social competence. Through reciprocal cascade loops, children who have slight early developmental advantages may make greater gains, while others may fall further behind.

In studying potential developmental cascades, it is also important to consider whether important child (and/or contextual) characteristics may modify the nature or extent of such processes. In particular, co-morbid nonverbal intellectual delay in children with ASD may be an added genetic or epigenetic "hit" that may further disrupt dynamic interactions between the developmental pathways of different domains over time (Elsabbagh & Johnson, 2010; Mundy, et al., 2007). Conversely, children with ASD who function within the unimpaired or "normal" cognitive range of abilities may demonstrate a greater ability to compensate for initial impairment – e.g. they may be better able to use enhanced language abilities to further improve upon their social understanding. For example, Ferrer & McArdle (2010) found that children with dyslexia who were better able to compensate for their disability compared to others demonstrated stronger "developmental coupling" associations between IQ and reading abilities over time -- the two domains or abilities were more strongly linked among children who were better readers (Ferrer et al., 2007). Similarly, children with ASD and higher nonverbal intellectual quotient (IQ; i.e. within normal range of > 70 SS points) may demonstrate stronger reciprocal developmental associations between the important domains of social competence and language.

Given the above, it is important to understand in more detail whether reciprocal effects occur between social competence (SOC) and language ability (LANG) early in the development of children with ASD, the extent to which they occur (the strength of association) and whether such patterns differ between clinically important groups of children. To date, studies of ASD have not addressed such questions. We aimed, therefore, to examine more closely how these two domains influence each other from one time point to another during an important period in their emergence.

As part of a larger prospective multi-site observational study of the development of children with ASD, we analyzed data from 365 children aged 2-4 years who had recently been diagnosed with any ASD. Longitudinal cross-lagged models – also known as reciprocal effects models (Marsh, Trautwein, Ludtke, Koller, & Baumert, 2005) – were developed using structural equation modeling with data from 3 time points: baseline (within 4 months of diagnosis, or T1), 6 months- (T2) and 12 months (T3) later. Such models incorporate a stability path for each construct and cross-domain associations within each time point (within-time correlations) and between time points (e.g. baseline SOC [SOC_1] to LANG at Time 2 [$LANG_2$]). We hypothesized that language and social competence would exert reciprocal influences over time: i.e. greater baseline SOC would be associated with stronger LANG measured at T2, which in turn would be associated with improved SOC at T3, and its complementary pattern. Furthermore, in keeping with the claims of social orientation theories – that advantages in early social competence would predict higher language levels -- we expected a stronger association between SOC at time of diagnosis and LANG 6 months later than between baseline LANG and later SOC. Finally, we compared the strength of associations between social competence and language within the reciprocal effects model between two subgroups of children: those who scored below versus above a cut-off of 70 SS points on nonverbal cognitive testing. We expected that preschoolers with higher cognitive functioning would demonstrate stronger reciprocal effects than less cognitively capable children.

METHODS

Participants

Data were obtained from a Canadian multisite longitudinal inception cohort study of 2- to 4-year-olds diagnosed with any ASD (autistic disorder, Asperger Disorder, pervasive developmental disorder-NOS [PDD-NOS]) in the previous 4 months. Participants presented for initial assessment at major ASD centres in Halifax, Montreal, Toronto, Hamilton, Edmonton and Vancouver. Inclusion criteria comprised: DSM-IV diagnosis of ASD or autistic disorder, Asperger Disorder or PDD-NOS as determined by clinical judgment of an interdisciplinary team with diagnostic expertise; fulfillment of criteria for ASD according to both the ADOS (semi-structured standardized assessment of the child; Lord et al., 1989, 1999) and ADI-R (semi-structured parent interview, Lord, Rutter & LeCouteur, 1994) using the Risi et al., (2006) criteria. Children were excluded if they had a known genetic syndrome or neurological basis for disorder or if the parents did not speak English or (in Montreal) French (prohibiting engagement in testing).

Measures

The *ADI-R* (Lord, Rutter, & Le Couteur, 1994) is a semi-structured parent interview that assesses developmental abilities and behaviors related to DSM-IV-TR diagnostic criteria for ASD (APA, 2000). Items are scored from 0 (no autism-specific abnormality present) to 3 (extreme abnormality indicative of autism).

The ADOS (Lord et al.,2000) is a semi-structured, standardized assessment in which a trained clinician engages a child in activities developed to assess social and communication behaviors indicative of DSM-IV-TR symptoms of ASD (APA, 2000).

Preschool Language Scale-4th Edition (PLS-4; Zimmerman, Steiner & Pond, 2002).

The PLS-4 is an individually administered task used to identify children with language disability. It provides scores for Total Language (TL), Auditory Comprehension (AC) and Expressive Communication (EC) for children from birth through age 6 years, 11 months, or those who are functioning developmentally in that range. The AC subscale evaluates how much a child understands, and targets nonverbal skills such as attention to speakers as well as basic vocabulary, concepts and grammatical markers. Raw scores were used to facilitate interpretation of cross-domain associations and stability of the scores over time. For the purposes of the present study, the PLS-4 scores of these children were considered censored at that time point and imputed using procedures described in Study 1. If a child failed to reach a ceiling level on the PLS-4, research staff also administered the Clinical Evaluation of Language

Fundamentals (CELF; Wiig, Secord, & Semel, 1992) at the same time point). At successive time points, the child would be administered only the CELF.

The Vineland Adaptive Behavior Scales, Second edition (Sparrow, Cicchetti, & Balla, 2005)

The VABS-II is a semi-structured interview designed to assess personal and social sufficiency of individuals from birth to adulthood. It measures an individual's strengths and weaknesses in socialization, communication and daily living skills in children aged 0 to 18 years, 11 months .An assessor interviews a respondent most familiar with the child's behavior, and rates whether a child performs a given developmental task on a scale from 0 - 2 ("never" to "usually"). Higher scores demonstrate superior adaptive behavior skills. The Socialization subdomain scales used in this study were: Interpersonal Relationships ("How the individual interacts with others", 38 items), Play and Leisure Time ("How the individual plays and uses leisure time", 31 items) and Social Coping Skills ("How the individual demonstrates responsibility and sensitivity to others", 30 items). Raw scores were used in order to facilitate interpretation of longitudinal associations within the structural equation model.

Merrill-Palmer-Revised Scales of Development (M-P-R; Roid & Sampers, 2004)

The M-P-R is an individually administered measure of intellectual development that is appropriate for children aged 2 to 78 months. The Cognitive Domain score, a measure of nonverbal intellectual ability, was used to divide the sample into two subgroups for use in multi-group analyses. In order to characterize children with and without co-morbid intellectual disability, two subgroups were created to compare children who scored below versus above a cut-off of 70 standard score points. For consistency, these groups are referred to as less- versus more "cognitively able" children with ASD.

Analyses

Measurement Model

The development of measurement models for emerging social competence and language ability is described in detail in Chapter 2.To summarize, two latent variables were developed to represent social competence (SOC) and language ability (LANG) at three time points: baseline (T1), 6 months- (T2) and 12 months later (T3). The latent SOC variable represented the shared variance among three indicators – the observed scores of the VABS-II Socialization domain subscales – Interpersonal Relationships, Play and Leisure and Social Coping; the factor loadings were of appropriate size (0.69 to 89, $p<0.001$) and the overall fit for this model across all time points was excellent. Furthermore, the factor loadings were invariant across time points and between the subgroups of interest in this study (that is, children above and below the median scores for baseline age and IQ). Therefore, in this model, factor loadings for the same indicators were constrained to equal each other across time points and between subgroups. Error covariances linking residual error terms for the same indicators over time (e.g. VABS-IR at T1, T2, T3) were allowed to vary freely in this study (i.e. they were not constrained to equal each other).

In Chapter 2, which described the development of the measurement model, the PLS-4 was used to develop a latent variable for emerging language ability, with the Auditory Comprehension (AC) and Expressive Communication (EC) subscale scores as indicators. Despite excellent model fit, the standardized factor loadings across all time points were above 0.90 in this sample, suggesting that the scores were highly collinear and so highly correlated as to be interchangeably representative of language ability. Therefore, the observed AC score was used instead of a latent variable to represent emerging language, with freely varying covarying error terms across time points.

Structural Model

The cross-lagged structural model, also known as path analysis, builds on the above measurement model by examining linear relationships of hypothesized direction between the SOC latent variables and the observed LANG variable at T1, T2 and T3 (See Figure 1). In keeping with the hypothesis of reciprocal effects, the model outlines a series of regression weights with two patterns: (a) stability paths linking the same construct across time points; (b) within-time cross-domain correlations measured at one time point (i.e. SOC_1-$LANG_1$); and (c) cross-lagged paths from one construct at a given time point (e.g. SOC_1) to the other at the following time point (e.g. $LANG_2$). Thus, cross-lagged models enable one to test for reciprocal cross-domain associations while controlling for earlier effects of SOC or LANG building on themselves over time. Furthermore, disturbance terms at T2 and T3 represent residual or unexplained variance in SOC and LANG. The strength and statistical significance of each regression weight parameter were estimated, as was the overall goodness of fit of the model. The following goodness of fit tests were used: the Tucker-Lewis Index (TLI) and Comparative Fit Index (CFI; values ≥ 0.95 = excellent fit), the Root Mean Square Error of Approximation (values ≤ 0.05 = excellent fit, 0.05-0.09 = good fit, and over 0.10 = inadequate fit (Hu & Bentler, 1999). The chi-square test of fit is often considered to be excessively stringent in the presence of large sample sizes, but was included for completeness (Cheung & Rensvold, 2002); non-significant chi-square values ($p > 0.05$) reflect excellent fit.

The hypothesized regression model was then compared to a null model, which specified a complete absence of cross-lagged effects between social competence and language domains. The presence of significant cross-lagged parameter estimates and a significantly superior fit ($p < 0.05$) for the hypothesized model over the null model would support our initial hypothesis that reciprocal cross-lagged associations exist between social competence and language domains over time. The strength of cross-lagged paths from SOC to LANG versus those in the opposite direction was compared by examining the size and statistical significance of the unstandardized estimates, and also by constraining the paths of different directions to equivalence (i.e. the strength of the path from SOC at T1 (SOC_1) to LANG at T2 ($LANG_2$) equals the strength of the path from $LANG_1$ to SOC_2). A significant improvement of the model's fit, represented by a significant change in the χ^2 value ($\Delta\chi^2$, $p<0.05$) when relaxing the constraints (i.e., reverting to the hypothesized model) would indicate that the opposing paths were not equally strong, confirming our hypothesis that SOC_1-$LANG_2$ was the stronger of the paths. The size of the stability pathway coefficients between domains and across time points and cross-domain disturbance correlations across time points were also compared in this manner.

Multi-group comparisons were then performed to determine whether the stability paths or cross-lagged associations outlined in the hypothesized model differed between children with lower versus- higher cognitive scores (MPR-CD score < 70 and ≥70 SS points). To examine whether particular parameters (i.e. individual regression coefficients) were equal in size between groups, the fit of a nested model in which the parameters of interest were constrained to equivalence between groups was compared to the baseline hypothesized model in which the parameters were free to vary. A significant difference in χ^2 values ($p<0.05$) would indicate significant differences in the size of the parameters. The following parameters were examined in this way: a) baseline correlations between SOC_1 and $LANG_1$; b) individual cross-lagged regression paths across all time points (e.g. SOC_1-$LANG_2$, $LANG_1$-SOC_2 etc.), c) individual stability coefficients for SOC (i.e. SOC_1-SOC_2; SOC_2-SOC_3) and LANG ($LANG_1$-$LANG_2$; $LANG_2$-$LANG_3$). The same constraints and comparisons were carried out in subgroups

AMOS 17.0 was used and the models were estimated using maximum likelihood estimation (Arbuckle, 2006). Missing variables were imputed using multiple imputation techniques in order to include variables that might predict missingness but that were not present in the structural equation models. Five imputed datasets were created -- details of the predictors and variables included in the dataset are reported elsewhere (see Study 1). Structural equation models were run for each dataset separately, and the parameter estimates and standard errors were pooled using NORM software (Schafer, 1999). Because AMOS does not pool goodness-of-fit estimates across imputed datasets, the range of fit estimates is reported for each model and a range of $\Delta\chi^2$ tests. The size of parameter estimates was considered to differ significantly between subgroups if a constrained model was found to represent a significantly worse fit to the underlying data in at least 4/5 datasets. Unstandardized regression coefficients were used as estimates of the size of stability and cross-lagged paths, particularly to compare strength of estimates, and are reported as such unless otherwise specified.

RESULTS

Descriptive statistics of the sample are outlined in Tables 1 and 2. As demonstrated in Table 2, children with cognitive scores below 70 SS points on the MPR-CD also had significantly lower language and VABS-II Social Composite scores than those who scored at 70 SS points or above.

Hypothesized Structural Model, Entire Group.

The hypothesized model demonstrated an excellent fit to the underlying data (CFI=0.99-1.0; TLI=0.99; RMSEA=0.03-0.05), and explained a substantial amount of variance in SOC (77.3%) and LANG (81.8%) at T3. Social competence and language were moderately to highly correlated at baseline, with a mean $r = 0.74$, $p < 0.01$. The cross-domain T2 correlation was smaller (φ=11.79(2.40), r=0.35, p<0.01) and the T3 correlation was not significantly different from zero (φ=5.54(3.72), p=0.17, r=0.16) (See Table 3). As expected, given results from the development of the measurement model, all factor loadings for SOC_{1-3} were statistically significant and ranged from standardized regression weights of 0.69 (Social Coping) to 0.88 (Interpersonal Relationships; factor loadings not shown in tables). Analysis of the patterns of associations within and between SOC and LANG across T1-T3 yielded the following results: First, SOC and, in particular, LANG were highly stable over time -- An increase of 1 SD in $SOC_1$was associated with an increase of 0.47 SD in SOC_2, and an increase of 1 SD in SOC_2 was associated with an increase of 0.78 SD in social competence at T3 (see Table 3). There was no significant difference between the strength of the SOC stability regression across time points suggesting that the rate of change of social competence was positive and linear (see Table 4). Stability was also high for LANG, with standardized regression weights of 0.79 (p<0.01) from T1-T2 and 0.80 from T2-T3. Language ability appeared to be more stable than social competence over time; when the stability regression paths for SOC_{1-3} and $LANG_{1-3}$ were constrained to equality between domains there was a statistically significant worsening of fit in 5/5 datasets (See Table 4).

Despite the high stability of SOC and LANG constructs over time, small and positive but statistically significant cross-lagged paths were found in both directions across most time points (see Table 4). For example, an increase of 1 SD in SOC_1 was associated with an increase of 0.13 SD in $LANG_2$, and an increase of 1 SD in $LANG_1$ was associated with an increase of 0.37 SD in SOC_2. SOC_2 was then positively significantly associated with $LANG_3$ (B=0.21(0.09, p=0.02; β=0.14). However $LANG_2$ was not significantly associated with SOC_3 (B=0.12(0.07, p=0.12). There was a significant worsening of fit of the model when cross-lagged paths were constrained to zero, although comparison of nested models failed to indicate significant differences in strength between reciprocal SOC-LANG and LANG-SOC at any time point. Thus, small but significant cross-lagged effects were evident from SOC to LANG across all time points and from LANG to SOC at baseline-T1. However any differences in the strength of these reciprocal associations were unapparent according to χ^2-based tests of statistical significance.

Group comparisons: On the whole, relatively few differences existed between the groups of interest in this study. Contrary to our hypothesis, there were no significant differences in the strength of reciprocal cross-lagged effects or stability effects between children who differed by cognitive score-status with one exception. LANG1 was more strongly associated with SOC2 in children who scored lower than 70SS points on the MPR-CD as a group, compared to those who scored higher in 4/5 datasets ($\Delta\chi^2$=2.96, p=0.09-5.29, p=0.02) . Furthermore, across all datasets in children who scored higher than 70 SS points on cognitive testing (as compared to those who scored below), baseline correlations between SOC_1 and $LANG_1$ were significantly stronger than in children with lower cognitive scores ($\Delta\chi^2$ = 5.41, 1 df, p=0.02 – 7.68, 1df, p<0.01).

DISCUSSION

This study aimed to determine whether social competence and structural language were reciprocally related in the first year after diagnosis of very young children with ASD. We found that each domain was highly stable over time – children who, at time of diagnosis, scored either high or low on the social subscales of the VABS-II and the auditory comprehension scale of the PLS-4 relative to the rest of the sample were likely to maintain this standing over the ensuing assessments 6- and 12 months later. Although significant reciprocal effects were found between social competence and language ability across most time points (with the exception of T2 language to T3 social competence), they were generally very small. Furthermore, within-time correlations between social competence and language at each time point diminished across the time points. Finally, there were no significant differences in the cross-lags between subgroups within the sample divided by a “normative” cognitive score cut-off of 70 SS points on the MPR-CS, with two exceptions: social competence and language factors were more strongly correlated at baseline in the more cognitively able group, and language ability at T1 was more strongly associated with social competence at T2 in less cognitively able children compared to cognitively higher-scoring peers.

Evidence that the associations between social competence and language are small and appear to be weakening over time is not supportive of a reciprocal cascades model of development in the year after diagnosis. Rather, this pattern of findings is more consistent with two developmental pathways that are “pulling apart” over time as abilities become more specialized and build upon themselves. Indeed, the auto-regressive associations emphasized the significant stability of social competence and language as measured in this study in the first year after diagnosis. This resembles a recent study’s findings that typically developing children demonstrated very strong stability of language skills between the ages of 20 and 48 months (Bornstein & Putnick, 2012).

Small cross-domain effects were consistent from social competence to later language ability, and a reciprocal cascade was identified from baseline language to T2 social competence back to T3 language ability. Stronger social competence skills were associated with better language abilities 6 months later. Children with stronger baseline language abilities at time of diagnosis were more likely to have stronger social competence 6 months later (controlling for baseline social competence), which in turn was associated with improved language 12 months after diagnosis. Stronger social competence around time of diagnosis was associated with better language abilities at T2, 6 months later, although this did not then reciprocally extend to improved social competence at T3. Contrary to our hypothesis, the associations between baseline language and later social competence were as strong as those from social competence to later language.

Furthermore, children with ASD who scored within the “normal range” on cognitive testing were not statistically differentiated from lower-scoring preschoolers in the sample by stronger cross-domain coupling after diagnosis, but instead by stronger baseline correlations between social competence and language at time of diagnosis. Thus, nonverbal cognitive ability therefore appears to moderate this baseline cross-domain association. It has been argued that differential cross-domain associations between groups in developmental disabilities research are important, and that weaker correlations between abilities in developmentally disabled children (e.g. compared to TD children) may reflect signify that cognitive systems are not causally interacting in the same manner between groups (Thomas, Purser, & Van Herwegen, 2012). By extension, a possible inference from the present study’s findings is that children with ASD who lack the “added hit” of co-morbid intellectual disability may benefit from greater cross-domain developmental cascades prior to subsequent specialization of social and language pathways. Stronger associations between social competence and language may indicate a compensatory process that occurred earlier in development among more cognitively able children, in which processes of brain adaptation restore a developmental trajectory that is more normative (i.e. "higher-functioning" socially, linguistically) (Elsabbagh & Johnson, 2010).

Cognitive ability may also represent a third causal factor that influences both social and language development in a similar way, for example as a marker of brain plasticity or a child's capacity for learning from their environment. . Children who are more intellectually able may be better able to scaffold learning from one domain to another, for example to use language skills to reason through social situations. Such inferences are preliminary, however. Further research should ask similar research questions tested during earlier periods of development.

The results of this study may inform intervention practice and policy in the following ways: First, the strong stability and decreasing inter-relatedness of social and language development after diagnosis (i.e. at age 3-5 years) suggests that young children with ASD should have access to social competence *and* language interventions based upon their individual profiles of strengths and difficulties. Otherwise, language interventions may have diminishing returns for social skills over time. Secondly, the current study findings suggest that early intervention should target all children with early delays or atypicalities in emerging social competence (e.g. poor joint attention, little interest in social play or reciprocal interactions).It may be too late to wait for a formal diagnosis of an ASD before intervening if one wants to optimize potential developmental cascades. The stronger baseline cross-domain correlations across all children with ASD at time of diagnosis support claims that social competence-based interventions should be offered as early as possible (Dawson, 2008; Dawson & Zanolli, 2003; Kasari, Gulsrud, Freeman, Paparella, & Hellemann, 2012). More specifically, optimal spillover benefits from such interventions on language development may occur earlier in the toddler years. Early interventions should therefore target key developmental milestones instead of specific disorders. Such efforts would require significant public investments into early detection and intervention for all neurodevelopmental disorders (e.g. ASD, global intellectual delay, language impairment), and research into their effectiveness.

To our knowledge, this is the first study to examine longitudinal cross-lagged relations between developmental domains over time in children with ASD, using data from a very large prospective inception cohort. The results of this study are preliminary, and several limitations should be highlighted. First, the findings are correlational and do not provide conclusive evidence of causal associations. Secondly, latent variables should ideally be constructed from multiple measures with different informants and methods in order to minimize bias in associations between variables. The VABS-II is a parent interview and the PLS4 is a combined parent interview and direct assessment of the child – if the child is preverbal, the parent provides much of the information. Thus, some method or informant effects may have influenced the results, although this may be less problematic across lags of 6 months compared to cross-sectional associations. Third, we were unable to covary service uptake by children and families in this sample, however, we would not expect this to affect our questions of interest regarding developmental interactions. Fourth, cross-lagged panel designs examine inter-individual differences in stability and cross-domain associations between levels of variables across a sample of individuals, but not intra-individual change over time or variability within the sample. This study was therefore unable to examine whether reciprocal effects occur between initial levels and change in social competence and language over time, a question that would require a latent growth-curve modeling approach. Finally, the time points in this study were fixed at 6 months apart – it is possible that this time lag duration is either too short or too long to detect stronger cross-lagged reciprocal associations.

Future studies may build on the findings generated by this study. For example, given the strong stability of language, it may be most appropriate to investigate the effects of early social competence on growth or change in language using growth curve modeling. Incorporating measures of nonverbal IQ in a more dynamic way (e.g. as a predictor or lagged variable) may allow for a more nuanced understanding of its role in the growth and change of other domains. Finally, extending studies of reciprocal developmental associations in children with ASD earlier to capture emerging process in at-risk populations (e.g. infant siblings of children with ASD) and later on into school-aged years would enable researchers to examine larger patterns of effects between these and other domains across developmental periods, and to link these to relevant "real-world" outcomes, such as peer relationships, co-morbid mental health and academic or vocational success. Longer-term views would also enable us to examine developmental continuity and discontinuity in dynamically linked trajectories across developmental stages. Understanding when developmental cascades occur and how they are influenced by child, family and contextual factors will be important to the provision of more effective and developmentally sensitive interventions.

In conclusion, early social competence and language ability in children recently diagnosed with ASD are strongly correlated at time of diagnosis. These domains then appear to diverge in their development rather than building off each other reciprocally to any large extent. Children with ASD and average- or higher-range cognitive abilities may have received some developmental benefit from earlier cross-domain associations in the period prior to diagnosis. Future research might address this issue by studying high-risk infants and appropriate control groups. Overall, reciprocal cascade models analytic modeling techniques are promising tools for testing interactive developmental pathways in ASD and may help guide the implementation of more developmentally sensitive interventions.

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TABLE 1: Baseline (T1) Sample Characteristics

Gender	Age at diagnosis in months (mean, SD)	Merrill-Palmer Cognitive Score (mean, SD)	VABS Social Standard Score (Mean, SD)	PLS-4 Expressive Communication Standard Score (Mean, SD)	PLS-4 Auditory Comprehension Standard Score (Mean, SD)	ADOS Severity Metric (Mean, SD)
M=305 F=60	38.21(8.48)	57.29(24.65)	72.24(9.02)	65.12(19.89)	69.78(17.13)	7.67(1.65)

TABLE 2: Baseline Sample Characteristics, by Subgroup

	ADOS Severity Score	M-P-R Cognitive Score SS	Child Age at Diagnosis (mo.)	VABS Social Standard Score	PLS-4 Expressive Communication Standard Score	PLS-4 Auditory Comprehension Standard Score
Baseline cognitive ability (Score lower or higher than 70 SS points on MP-R CS)						
Less Cognitively Able (<70 SS)*	7.63(1.67)	44.57(14.90)	37.06(7.60)	70.34(8.34)	63.10(11.04)	56.59(11.25)
More cognitively able (70+ SS)*	7.43(1.59)	88.58(17.08)**	41.48(9.61)**	77.31(8.82)**	87.61(17.74)**	87.91(20.04)**

* Merrill-Palmer-Revised Cognitive Standard Score

**: Significant difference of means (independent samples T-test) for age and cognitive score groups, $p < 0.05$

TABLE 3. Unconstrained cross-lag model, entire sample.

	Parameter Estimate (SE)	**Standardized Parameter Estimate**	**p-value**
Regression Coefficients (B)			
T1 Social Competence→ T2 Social Competence	0.64(0.09)	0.47	P <0.01
T2 Social Competence → T3 Social Competence	0.79 (0.14)	0.78	P<0.01
T1 Language → T2 Language	0.92 (0.05)	0.79	p<0.01
T2 Language → T3 Language	0.86 (0.06)	0.80	P<0.01
T1 Social Competence → T2 Language	0.25 (0.08)	0.13	P<0.01
T1 Language → T2 Social Competence	0.27 (0.05)	0.37	P < 0.01
T2 Social Competence → T3 Language	0.21 (0.09)	0.14	P =0.02
T2 Language → T3 Social Competence	0.12 (0.07)	0.16	P = 0.12
Covariance Parameters			
ϕ SOC_1-$LANG_1$	56.18 (5.32)	r= 0.74	P<0.01
ϕSOC_2-$LANG_2$	11.79 (2.40)	r= 0.35	P<0.01
ϕSOC_3-$LANG_3$	5.54(3.72)	r=0.16	P=0.12
Goodness of Fit Tests	**χ2, 42 df**	**CFI/TLI**	**RMSEA (CI)**
Imputation #1	67.74,p<0.01	0.99/0.99	0.04 (0.02-0.06) pclose=0.79
Imputation #2	59.84, p=0.04	1.0/0.99	0.03(0.01-0.05) pclose=0.92
Imputation #3	55,13, p=0.08	1.0/0.99	0.03(0.00-0.05) pclose=0.96
Imputation #4	55.17, p=0.08	0.98/0.98	0.03(0.00-0.05) pclose=0.96
Imputation #5	75.43, p<0.01	0.99/0.99	0.05(0.03-0.06) pclose=0.60

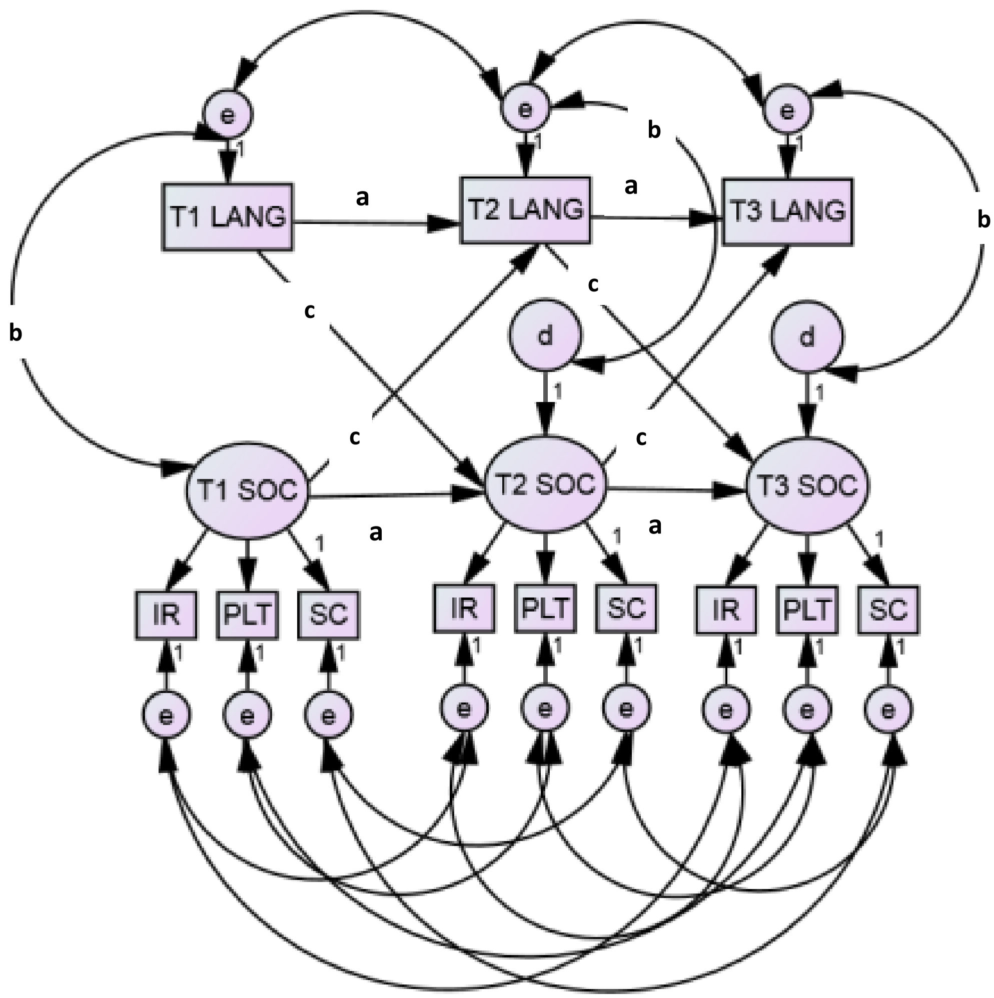
ϕ=covariance; r=correlation

TABLE 4. Goodness of Fit, Entire Sample, Comparison of Various Constraint Conditions.

	Range of Chi-square Difference Tests Across 5 Imputed Datasets, Compared to Unconstrained Model	# datasets in which Chi-square difference test statistically significant, p<0.05
Cross-lagged Coefficients =0	75.57, 4df, p<0.01-94.69,4df, p<0.01	5/5
SOC Stability Path = LANG Stability Path	7.66,2df,p=0.02-12.00, 2df, p<0.01	5/5
SOC1-LANG2 = LANG1-SOC2	0.003, 1df, p=0.96-0.18, 1df, p=0.67	0/5
SOC2-LANG3 = LANG2-SOC3	0.52, 1df, p<0.47-2.85, 1df, p=0.09	1/5
SOC1-SOC2 = SOC2-SOC3	0.70, 1df, p=0.40-2.85, 1df, p=0.09	0/5
LANG1-LANG2=LANG2-LANG3	0.09, 1df, p=0.76-1.44, 1df, p=0.23	0/5

Figure 1: Cross-lagged Model.

e= measurement error; d=disturbance (residual error); IR = VABS-II Interpersonal Relationships; PLT = VABS-II Play and Leisure time; SC = VABS-II Social Coping.
a= auto-regressive stability pathways; b= within-time cross-domain correlations; c=cross-lagged correlations
SOC = Social Competence; LANG =Language Ability



CHAPTER 4

STUDY 3:

TITLE: Developmental Cascades in ASD: A Dual-Domain Latent Growth Curve Approach

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CONTEXT AND IMPLICATIONS: The third study of this ‘sandwich thesis’ builds on the results of Study 2 that suggest that social competence and language pathways become more specialized in the first year after diagnosis of ASD in toddlers and preschool-aged children. By using a different longitudinal modeling approach -- latent growth-curves -- this study incorporates estimates of rates of change in social competence and language domains, and the extent to which growth in one domain influences change in another. This study was also able to describe whether trajectories differed between cognitively higher- versus lower groups of children with ASD. It therefore offers a different – and complimentary -- developmental snapshot of interactive developmental cascades between social and language trajectories in very young children with ASD.

This study is the first to model simultaneous developmental trajectories in a large, representative sample of young children with ASD. It found that, on average, children in the Pathways Study made notable gains in social and language skills in the first year after diagnosis but there was significant variation with respect to rates of change. Children whose cognitive abilities were in the "normal" range made greater language -- but not social -- gains than did children with co-morbid intellectual disability. Social competence at time of diagnosis, and its rate of change, were significantly associated with rate of change in language ability, however the converse was not true. In this study, baseline language ability was not predictive of change in social competence in the first year after diagnosis. This study adds important insights to the growing literature favouring early social competence-based interventions, and provides important models for further examination of developmental pathways in ASD.

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Abstract

Objectives: How quickly individuals with ASDs develop skills in one developmental domain [e.g., social competence (SOC)] may affect the rate of acquisition of multiple abilities [e.g., language (LANG)] in a cascade-like fashion. Uncovering how such dynamic processes might occur is crucial to developing more effective interventions. We aimed to: a) determine whether SOC and LANG varied significantly in a cohort of preschoolers with ASDs; and b) model dynamic interactions between SOC and LANG trajectories using latent growth curve analysis. **Methods:** Data for 365 2- to 4-year-olds were obtained from a prospective longitudinal study of preschoolers recently diagnosed with an ASD. Children were assessed at time of diagnosis and then twice at 6-month intervals using the Vineland Adaptive Behavior Scale II and the Preschool Language Scale 4. Models were developed to measure the associations between initial levels (intercepts) and rates of change (slopes) of SOC and LANG. **Results**: Children in this sample showed notable growth in SOC and LANG over 12 months. Initial levels and rates of change in LANG and SOC varied significantly between individuals. The intercept and slopes of SOC predicted the rate of change of LANG. Initial LANG did not predict change in SOC in the overall sample. Children with lower cognitive scores at base line demonstrated significantly slower LANG growth, and baseline

LANG was more strongly predictive of SOC than it was for more cognitively able children.

Conclusions: Early SOC and its growth appear to be more predictive of change in LANG than vice-versa. However some associations appear to be moderated by cognitive ability. These findings support early ASD intervention focusing on social competence with additional interventions tailored to children's individual developmental profiles.

BACKGROUND

Autism spectrum disorders (ASDs) are neurodevelopmental disorders characterized by common core impairments in social reciprocity and communication as well as restricted interests and stereotypic or repetitive behaviors. However, considerable inter-individual variability across the lifespan exists with respect to severity of core symptoms, associated cognitive and language deficits and adaptive functioning. As well, recent longitudinal studies of growth trajectories have also signaled that within ASD, individuals differ not only in their phenotypic expression at any one time but also across time as well (Anderson et al., 2007; Anderson, Oti, Lord, & Welch, 2009; Fountain, Winter, & Bearman, 2012; Munson, Faja, Meltzoff, Abbott, & Dawson, 2008; Sigman & McGovern, 2005). In fact, ASD has been described as a disorder that may be, at its essence, a convergence of disordered trajectories across multiple developmental domains (Tager-Flusberg, 2010). Understanding how such trajectories vary during sensitive developmental periods is important so that interventions that enhance the learning and well-being of individuals with ASD can be more effectively tailored.

Longitudinal studies have yielded important information about the early factors that contribute to greater developmental change. However, it is not known how change in one domain influences change in another. Although early social-cognitive impairment is a hallmark of ASD, there is nevertheless very early heterogeneity in children's emerging social competence skills, such as orienting to faces, engaging in joint attention and interacting with others in a reciprocal manner (Kuhl, Coffey-Corina, Padden, & Dawson, 2005). Young children with ASD who demonstrate relative advantages with respect to these foundational social skills appear to become better early language learners than those who demonstrate more difficulties in this domain (Charman, 2003; Mundy, Sigman, & Kasari, 1990; Sigman & McGovern, 2005; Toth, Munson, Meltzoff, & Dawson, 2006; Toth, Munson, Meltzoff, & Dawson, 2006). Early language ability in turn is a strong predictor of a range of later outcomes including symptom burden and adaptive functioning (Anderson, et al., 2009; Bennett et al., 2008; Szatmari et al., 2009; Venter, Lord, & Schopler, 1992). In this way even slight advantages in early social competence may have cascading effects on growth and change across multiple developmental trajectories through the development of language abilities.

This study attempts to address this issue by describing the simultaneous growth trajectories in social competence and language domains, and the dynamic associations between them. Better understanding of the relations between early social competence and emerging language development would enable us to consider whether one domain – that is, social competence or language -- is the greater constraint on development in the other. Furthermore, the associations between these trajectories may differ depending upon child characteristics, such as cognitive ability.

The objectives of this study are to determine: a) the rate of change in social competence and language ability in a sample of children with ASD aged 2-4 over the course of the first year after recent diagnosis; b) the extent of inter-individual variability in initial levels and rates of change in these domains; c) whether cross-domain interactions occurred over time; d) differences in social competence and language trajectories between children of higher- versus lower- cognitive ability; and e) child- and family-level predictors of developmental trajectories in each domain.

A latent growth curve (LGC) modeling approach was used to examine the simultaneous association between latent variables representing the baseline levels (intercepts) and rates of change (slopes) in social competence and language. We hypothesized that early social competence scores (SOC) would be associated with initial level and rate of change in language ability (LANG). Early language abilities in turn would also predict, albeit less strongly, rate of change in social competence. Furthermore, we expected that children who improved more rapidly with respect to their early social skills would show more dramatic language gains as well.

METHODS

Sample

The initial sample consisted of 365 newly diagnosed preschool children with ASD participating in the "Pathways in ASD" Study, a Canadian multisite longitudinal study. Inclusion criteria were: a) clinical diagnosis of ASD made in the previous four months, confirmed upon enrolment with the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000), with the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter & LeCouteur, 1994) using the Risi et al. (2006) criteria and with diagnosis assigned by a study clinician using the DSM-IV-TR criteria; and (b) chronological age equal to or older than 2 years and younger than or equal to 4 years, 11 months. Children were excluded if they met any of the following criteria: (a) cerebral palsy or other neuromotor disorder interfering with study assessments; (b) any known genetic or chromosomal abnormality; or (c) severe visual or hearing impairments. Families were recruited from regional ASD assessment centres in five Canadian cities (Halifax, Montreal, Hamilton, Edmonton and Vancouver). Approval for the study was obtained from Research Ethics Boards at all sites and families gave their informed consent.

Children and families were assessed at three time points using a battery of measures at baseline (T1), 6 months- (T2) and 12 months (T3) later. Hypothesized predictor and outcome measures were included at each time point; 359 families (98.4%) had completed the Vineland at T1, 315 families had completed Time 2 (86.3%) and 298 had completed Time 3 (81.4%). For the language measures (Preschool Language Scale -4 [PLS-4] and Clinical Evaluation of Language Fundamentals [CELF]), 345 participants (94.5%) completed T1, 312 (85.5%) completed T2 and 291 (79.7%) completed T3. Thirty-five families dropped out of the study after enrolment, and 18 did not complete T2 data due to scheduling or other reasons, but returned for T3. There were no differences between study completers and those who dropped out based on child age at diagnosis, ADOS severity score, Vineland total score or PLS-language scores at T1.

Procedure

Children were assessed as soon as possible after enrolment in the study. All examiners/ interviewers were trained and supervised by clinicians with ASD expertise. For measures involving interpretation and scoring, all interviewers were trained by the same investigator using the same instructional video. Research staff met standard research reliability criteria for ADOS and ADI-R and all other measures prior to conducting assessments for the study.

Measures

The *Autism Diagnostic Inventory-Revised* (*ADI-R; Lord, Rutter & LeCouteur, 1994)* is a semi-structured parent interview that assesses developmental abilities and behaviors related to DSM-IV-TR diagnostic criteria for ASD (APA, 2000). Items are scored from 0 (no abnormality present) to 3 (extreme abnormality; Lord, Rutter & LeCouteur, 1994).

The *Autism Diagnostic Observation Schedule* (*ADOS*; Lord et al., 1989; Lord et al., 1999) is a semi-structured, standardized assessment in which a trained examiner engages participants in activities developed to assess social and communication behaviors indicative of DSM-IV-TR symptoms of ASD (APA, 2000); (Lord et al., 1989; Gotham, Risi, Pickles, & Lord, 2007). The ADOS severity metric (Gotham et al., 2007) enables comparison of the severity of autistic symptoms in children across levels of ability, and is scaled from 1-10.

Preschool Language Scale-4th Edition (PLS-4; Zimmerman, Steiner & Pond, 2002).

The PLS-4 is an examiner-administered measure used to identify children with language disability. It provides standard scores and age-equivalent scores for Total Language (TL), Auditory Comprehension (AC) and Expressive Communication (EC) in children from birth through age 6 years, 11 months, or those with developmental functioning equivalent to that range. Items designed for preschool children aged 2-4 assess comprehension of basic vocabulary, concepts and grammatical markers (Zimmerman & Castilleja, 2005). The AC subscale evaluates how much a child understands, and targets nonverbal skills such as attention to speakers as well as basic vocabulary, concepts and grammatical markers. The AC scale was used as a marker of overall language in the current study, as it was found to be very highly correlated with the Expressive Communication (EC) subscale of the PLS-4 and an adequate proxy for a latent variable combining the two subscales as indicators.

PLS-4 and subscales have good test-retest reliability (•=0.82 to 0.95) and internal consistency (=0.91-0.9; Zimmerman, Steiner & Pond, 2002), and are sensitive to change as well as to differences in language ability in samples of children with ASD (Volden et al., 2010; Zimmerman & Castilleja, 2005). Raw scores were utilized in the main hypothesized models, with standard scores used only to characterize growth in language ability. In the current study, research staff continued testing a child until a ceiling was reached according to testing guidelines; if a child progressed without reaching a testing ceiling at a given time point (i.e., performed beyond the limits of the PLS-4), then the Clinical Evaluation of Language Fundamentals (CELF; Wiig, Secord & Semel, 1992) test was also administered at that time point. At the following time point, only the CELF would be administered. In such cases, the PLS-4 score would be estimated using multiple imputation procedures.

The Clinical Evaluation of Language Fundamentals (CELF) (Wiig, Secord, & Semel, 1992)

The CELF is an examiner-administered tool designed to evaluate language deficits in children. In the current study, it was administered to children whose language abilities exceeded those evaluated by the PLS-4 (n=12 at T2; n=30 at T3), and was included only as a predictor in the multiple imputation models.

The Vineland Adaptive Behavior Scales, 2nd edition (VABS-II; Sparrow, Cicchetti, & Balla, 2005)

The VABS-II is a semi-structured interview designed to measure strengths and weaknesses in socialization, communication and daily living skills for children aged 0 to 18 years, 11 months old. It yields standard scores (mean =100, SD=15). An assessor interviews a respondent most familiar with the child's behaviour, then rates whether a child performs a given developmental task according to criteria on a scale from 0-2 ("never" to "usually"). Higher scores demonstrate superior adaptive behavior skills. In this study, the 38-item Interpersonal Relationships (VABS-II IR) subscale was used as a measure of social competence in order to analyse raw scores rather than the standardized score of the composite VABS-II Socialization domain in order to facilitate the interpretation of growth curves. Standardized VABS-II Socialization domain scores were analyzed only to give additional description of social competence and language growth in standardized score terms, not to test interactions between curves. In previous latent-variable studies using the same sample (Chapters 2 and 3) the observed VABS-II IR indicator variable loaded quite highly onto a latent variable using all three subscales of the VABS-II Socialization domain (standardized =0.80-0.95). This indicated that, in this sample, the IR subscale could serve as an adequate proxy for a social competence construct as indexed by the VABS-II.

Merrill-Palmer-Revised Scales of Development (M-P-R; Roid & Sampers, 2004)

This M-P-R is an individually administered measure of intellectual development that is appropriate for children aged 2 to 78 months of age. The Cognitive domain standard score is a measure of nonverbal intellectual ability. A score of 70 standardized score points (representing the cut-off for “normal” IQ) was used as a cut-off to create less- versus more cognitively able participant groups.

Aberrant Behavior Checklist (Aman, Singh, Stewart, & Field, 1985)

The ABC is a 58-item caregiver-report measure in which parents (in this study) are asked to report on their child’s behavior over the past 4 weeks. It comprises 5 subscales: a) Irritability (15 items), b) Lethargy/Social Withdrawal (16 items), c) Stereotypic Behavior (7 items), d) Hyperactivity/Noncompliance (16 items) and e) Inappropriate Speech (4 items). In this study, subscale scores were used as covariates in the LGC model.

Child Behavior Checklist, Preschool Version (CBCL: Achenbach, 1991)

The CBCL is a caregiver-completed questionnaire that addresses emotional and behavior problems as well as certain developmental and disabilities in children aged 1 ½ to 5 years old. Internalizing (36 items) and Externalizing scores (25 items) were used in this study as covariates in the final LGC model.

Primary Caregiver Educational Status

The primary caregiver rated his/her highest level of education attained on a scale from 1 (some high school) to 11 (doctorate or equivalent degree).

Household Income

The primary caregiver rated the family household income on a scale from 1 (< $5,000) to 11 (> $80,000). Income increments were $5,000 up to $20,000 and then increments were $10,000.

Missing data were imputed using the multiple imputation module in SPSS 20.0 (IBM Corp., 2011; for details see Supplementary Online Materials). The pooled parameter estimates and standard errors for the five imputed datasets were then computed using NORM software for missing data analysis (Schafer, 1999). AMOS cannot pool estimates of goodness of fit across multiple imputation datasets, therefore goodness of fit indices are outlined in the results section as a range of values, from least to most optimal fit, across all imputed datasets, and include the Tucker-Lewis Index (TLI; good fit • 0.90, excellent fit •95); the Comparative Fit Index (CFI; excellent fit • 0.95); and the Root Mean Square Error of Approximation (RMSEA; good fit =0.05=0.08; acceptable fit • 0.10; Hu & Bentler, 1999). The chi-square test of fit was also computed, but because it has been described as overly stringent and rejecting of well-fitting models with larger sample sizes, it was not included as criterion for goodness of fit (MacCallum, Browne & Sugawara, 1996).

Analytic Approach

The Latent Growth Curve (LGC)

Baseline Model 1

In this study, a baseline model was first developed to determine the mean baseline levels, or intercepts, and growth over time, or slopes, of social competence (SOC; represented by the observed variable VABS IR) and language (LANG; PLS4- AC). The average slopes and intercepts of each domain were calculated for the entire sample, as well as the extent to which these parameters varied between individual participants – that is, the variance of each intercept and slope. The growth model included two latent variable parameters for each domain: an intercept factor representing the individual's baseline score on SOC or LANG at T1, and a slope factor representing the individual's rate of change in each domain over one year (T1-T3). All factors were allowed to covary with each other.

Hypothesized Model 2

Our hypothesized model built on the structure of the first by including the same intercept and slope factors (see Figure 2). However, in this model, the associations between certain factors were specified in greater detail to test our hypotheses. Therefore, Model 2 outlined the following hypothesized paths, the strengths of which are estimated in the form of regression coefficients: 1) from the Intercept factor for SOC to the Intercept factor of LANG (i.e., baseline SOC is associated with baseline LANG); 2) from the Intercept of SOC to the Slope latent factor for LANG (i.e., baseline SOC is associated with linear change in LANG over time); 3) from Intercept of SOC to Slope of SOC (baseline SOC is associated with rate of change in SOC; 4) from the Intercept of LANG to the slope of LANG; 5) from LANG Intercept to Slope of SOC (i.e., initial LANG would be associated with rate of change in SOC); and 6) from SOC Slope to LANG slope (i.e., increased rate of change in social abilities would be associated with increased rate of change in language performance in the first year after diagnosis of an ASD). Disturbance terms for each factor were specified to estimate the residual variance that remained unexplained after accounting for the hypothesized relations between factors.

------------------------Figure 1 About Here ------------------------------------

To determine whether cognitive ability modified any of these relationships, Model 2 was tested separately in: a) children with T1 M-P-R Cognitive standard scores below and equal to or above 70 at T1 (referred to henceforth as lower- versus higher baseline cognitive ability). Each parameter estimate was separately constrained to equality between the two group conditions. This equivalence model was then compared to the original unconstrained model; a significant difference in size of the parameters of interest between the two groups would be indicated by a statistically significant ($p<0.05$) change in the chi-square (^{2}) goodness of fit test.

Finally, Model 3 then built on model 2 by testing individually, a number of covariates that might account, at least partially, for any residual variance in the Intercept and Slope factors for Social Competence and Language Ability for the sample as a whole (not depicted in figures). First, any paths from Model 2 that were not statistically significant were dropped from the model. Then, regression paths were drawn from each covariate at a time to the disturbance terms for the Intercept and Slope factors to determine the size, direction and statistical significance of any associations.

RESULTS

The sample was primarily male (n=305 boys) and lower-functioning with respect to cognitive ability (Mean M-P-R Cognitive standard score=57.29(24.65) (See Table 1). Most participants met criteria for autistic disorder (n=314, 86%) on the ADI-R. There were no differences with respect to symptom severity based on the ADOS severity metric. Children with M-P-R cognitive standard scores lower than the median of 70 also had significantly lower language scores as well as significantly lower VABS-II socialization scores.

Model 1, Baseline Model

As shown in Table 2, the baseline model outlined the mean intercepts, slopes and variance of the SOC and LANG variables. The overall fit of the model was excellent, with CFIs of 0.98-0.99 across all datasets, TLIs 0.97-0.99, and adequate RMSEA values of 0.06-0.09. The mean score for Social Competence, as indexed by the VABS-II IR, was 25.00 at T1, and increased at a rate of 8.87 raw score equivalents over the first year, on average. The intercept score for LANG was 26.79(0.61), which increased on average by 11.04 raw-score equivalents on the PLS4-AC for the entire sample over one year. Growth in standard score terms, using the standard scores for the Vineland Socialization domain and the PLS4-AC was as follows: the mean VABS Socialization standard score at T1 was 72.31(0.48), which increased at a rate of 3.05(0.57) standard score points over 12 months. Mean language ability for the group was indexed by 65.09 SS points on the PLS4-AC subscore, increasing at a mean rate of 9.5 SS points, which suggests that, on average, children in this sample were developing language skills at a rate faster than a normative sample. All slopes were statistically significantly greater than zero. The variance estimates indicated clinically important and statistically significant variability across the intercepts in the sample and slopes for Social Competence and Language ability in this sample: examining scores 2SD below and above the mean SOC and LANG slopes for the sample revealed that rates of change for social competence ranged from below a decrease of 4.33 raw points over 12 months to greater than 21.87 points on the VABS2-SIR. The slope for LANG ranged from a negative rate of change of over -7.08 raw points on the PLS-AC to an increase of 29.16 points. Therefore certain children appeared to be slowing with respect to their growth while others improved significantly (See Table 2).

Model 2, Hypothesized Model

The baseline scores for SOC and LANG at T1 were strongly associated with each other (standardized =0.76, $p<0.001$; see Table 3). The association between the intercept of Social Competence and its rate of change was non-significant, indicating that in the hypothesized model, initial social abilities did not significantly influence subsequent rate of change. However, there was a significant inverse association (standardized =-0.49, p<0.01) for language ability, indicating that, on average, the language trajectories of children with higher baseline PLS-4 scores were less steep than children with lower language at baseline. . Cross-domain associations were found: initial social competence abilities were moderately associated with increased rate of growth in language abilities (standardized =0.62, p< 0.05). However, there was not a statistically significant association between initial language and rate of change in social competence. The slope of social competence was moderately and significantly associated with the slope of language ability. The residual error variances indicated that there remained significant variability in all of the intercepts and slopes after accounting for the associations in this model, signifying that factors not included in this model likely account for variability in all growth parameters.

Multi-group Comparisons:

Lower- versus Higher Cognitive Functioning

Children who scored above 70 SS points on the M-P-R- Cognitive Score demonstrated higher baseline levels of SOC (• 2,1df = 65.59,p<0.01 to 67.70, p<0.01 for mean SOC intercept) and LANG (• 2 range, 1df = 112.26, p<0.01 to 119.41, p<0.01). There were no significant differences in rate of change of SOC (• 2, 1df = 0.43, p=0.51 to 5.49, p=0.02. However, children with higher M-P-R Cognitive scores made greater language gains (• 2 range, 1df = 4.01, p<0.05 to 15.01, p<0.01) (see

Table 4). There were no significant differences in the variances of the slopes of language or social competence between groups.

In Model 2, a somewhat different pattern emerged. Again, the intercepts of SOC and LANG were more strongly associated in children with M-P-R Cognitive score greater than 70 than those who were lower-scoring (• 2 range, 1 df = 4.00, p<0.05 to 4.82, p=0.03). In addition, the association between the LANG intercept and the slope of SOC was significantly stronger in the lower cognitive-functioning group compared to those with scores above 70 (• 2range, 1df = 5.75, p<0.01 to 16.38, p<0.01).

Model 3, Covariates.

Multiple covariates were evaluated to determine if child- or parent factors influenced the levels near time of diagnosis and rate of change over time for SOC and LANG. Child gender and ADOS severity score were not associated with unique variance in any of the parameters. Other child variables showed small and specific associations with different parameters (indicates unstandardized regression coefficients). Examination of atypical or challenging ASD-related behaviours as rated by parents using the ABC revealed the following associations: Greater stereotypy scores were associated with poorer baseline social competence scores (=-0.33(0.10), p<0.01). By comparison, children whose parents described them as being more irritable were more likely to show greater language ability shortly after time of diagnosis (unstandardized =0.18(0.06), p< 0.01). Behaviours indicating greater lethargy and social withdrawal were similarly associated with higher language ability at study baseline, as was greater hyperactivity (unstandardized =0.17(0.08), p=0.05 and =0.15(0.06), p=0.01, respectively). However, both behavior profiles also showed inverse association with social competence at baseline: greater lethargy and social withdrawal at baseline were significantly related to lower baseline social competence (=-0.27(0.05), p<0.001). Hyperactivity as rated by parents also demonstrated smaller but statistically significant inverse relations with baseline social competence (=-0.08(0.04), p=0.04). Therefore, preschooler lethargy/social withdrawal and, conversely, hyperactivity were both associated with poorer emerging social skills but greater language ability at time 1 of the study. There were no statistically significant associations between child covariates and slopes of social competence or language ability.

Finally, family characteristics were also associated with growth parameters after accounting for reciprocal associations between social competence and language: Family income was associated with higher levels of social competence shortly after time of diagnosis (=0.33(0.14), P=0.02). Primary caregiver education demonstrated borderline statistically significant associations with baseline language ability (=0.35(0.19), p=0.06) and positive, statistically significant associations with the slope of social competence (0.34(0.17), p=0.05) (See Table 5).

CONCLUSIONS

On average, the preschool-aged participants with ASD in this study made significant gains in social competence and language ability over the 12 months after they were diagnosed with an ASD. However, individuals varied significantly with respect to baseline abilities and rates of change over time; some children slowed down with respect to early language growth while others made remarkable gains. Considerable cross-domain interactions appeared to occur during a key developmental period for social and language learning. Specifically, initial social competence and its rate of change were moderately to strongly associated with increased growth in language ability over the following year. In contrast, language ability as measured near the time of diagnosis was not associated with significant change in social competence in the group as a whole. Rates of change in both domains were also strongly associated during that year, supporting a strong developmental coupling between domains.

These results support earlier findings that early social competence is a pivotal skill that may constrain growth in language ability (Charman, 2003; Dawson et al., 2004; Siller & Sigman, 2005). These analyses extend these findings futher: children with ASD who experience greater growth in social competence are more likely to experience better gains in language development, and the influence of social competence on later language growth appears to be more important than the converse effects of early language on the rate of social development in the preschool years. The importance of social competence as a key upstream developmental milestone is also supported by a recent follow-up study of 60 adults with average-range IQ who had been diagnosed with ASD during childhood. Among these individuals, early Reciprocal Social Interaction score on the ADI-R was the strongest predictor of a composite of adult functional outcomes, controlling for early language and cognitive ability (Howlin, Moss, Savage & Rutter, 2013).

Since language ability has also been extensively described as an important predictor of heterogeneity across multiple outcomes (Bennett et al., 2008; Szatmari et al., 2009; Venter, Lord and Schopler, 1992), development in this domain during the preschool years may be an important mediator between early social competence and other developmental trajectories. Future studies examining longitudinal mediation associations will therefore be essential to link all of the above findings together. To this aim, the dual-growth curve model described in the current study can be extended forward through childhood and adolescence, incorporating other developmental trajectories that are essential to the well-being and health of children with ASD.

This study is the first, to our knowledge, to compare how social competence and language trajectories change and interact in early childhood between cognitive-ability-based sub-groups of children with ASD. In this study, the less cognitively able children in this sample (M-P-R Cognitive standard scores below 70) had significantly lower social competence and language scores at baseline, and showed less in growth in language, but not social competence. However, among this lower-scoring group, baseline language ability was a stronger predictor of social competence gains than in the more cognitively able group. This may reflect a compensatory process among more intellectually disabled preschoolers. Furthermore, baseline social competence and language abilities were more strongly correlated in the more cognitively able group of children. This suggests that dynamic processes involving these domains, possibly moderated by nonverbal intellectual ability, may occur earlier the development of children with ASD, and may underlie heterogeneity in trajectories and outcomes. Such findings are preliminary, however, and will require replication and extension.

Furthermore, we found some similarities and differences with respect to child and parent covariates in this sample. Similarly to Charman et al. (2003), we found that degree of engagement in stereotypies around time of diagnosis did not predict language development, however in the current study greater stereotypies were concurrently associated with lower social competence scores. Greater levels of hyperactivity and social withdrawal were both associated with lower initial social competence levels but, interestingly, higher initial language scores, as was greater irritability. This difference in directionality of associations between child aberrant behaviours and social and language competency requires further exploration and replication, ideally using multiple different measures and multiple informants. However, it may indicate a difference in co-morbidity between more versus less verbal children. Alternatively, this may also reflect important measurement and reporting issues, for example that parents are more likely to recognize and report certain specific behaviours or in turn conceptualize them as “more aberrant” in more verbal children or intellectually capable children with ASD.

Finally, the socioeconomic context of very young children with ASD appears to make a difference. Greater family income was associated with greater baseline social competence in this sample. Furthermore, in keeping with earlier reports (Anderson et al., 2007), in this study, higher levels of primary caregiver education (primarily mothers) was associated with greater gains in social competence after diagnosis and its association with higher baseline language ability approached significance.

This study has several strengths, including the size of this inception cohort of children with ASD, the use of repeated measures across multiple time points, and the novelty and relevance of the analytic approach.

Several limitations must also be noted: First, the current study was limited to data reflecting 12 months of follow-up, and only three time points. Second, a small number (<10%) of more verbal children in this sample "outgrew" the PLS-4 at T2 or T3 and graduated to the CELF. We attempted to correct for this by using multiple cognitive and linguistic predictors to develop imputed PLS-4 values; however, the data may be biased somewhat towards children with lower language abilities. Third, multiple measures were not available for the constructs of interest, which increases the risk of method or informant bias. Finally, we were unable to incorporate variables addressing service use; this may have affected the multi-group comparisons if a certain subgroup were more likely to receive intervention than the other.

These findings offer several important implications for practice and policy. First, our results support those ASD theoretical frameworks and intervention approaches that favor targeting early social competence in order to leverage cross-domain learning cascades (Dawson et al., 2010; Kasari, Gulsrud, Wong, Kwon, & Locke, 2010; Koegel, Vernon, & Koegel, 2009; Landa, Holman, O'Neill, & Stuart, 2011). Although future intervention research with longer follow-up is needed, such an approach may optimize gains across multiple domains more efficiently by starting "upstream" and focusing on key developmental domains that may influence other developmental trajectories. Treatments should also be additionally tailored to child and family characteristics (e.g., cognitive ability, family resources) to minimize barriers to optimal treatment gains. Second, by the time of diagnosis, the relative developmental advantages or impairments experienced by children with ASD already affect growth in language ability. Along with cognitive ability, these domains have been shown in earlier studies to predict multiple other outcomes in later years (Bennett, et al., 2008; Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008; Szatmari, et al., 2009; Venter, et al., 1992). This argues against waiting for a formal diagnosis before intervening, for example by targeting toddlers showing significant social and language delays or differences. Many toddlers who do not go on to meet criteria for ASD on more stringent diagnostic testing nevertheless suffer from delays in social, language and cognitive development and may also benefit from early intervention (Glascoe, 2001; Wallace & Rogers, 2010). It may be that intervention best serves young children with ASD if it is tailored to phenotype rather than to diagnosis, if it can create gains in children's social competence during the toddler years and if it is offered to a broader range of children who are at developmental risk of falling further behind.

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TABLE 1: Baseline (Time 1) Sample Characteristics

Gender	Age at diagnosis in months (mean, SD)	Merrill-Palmer Cognitive Score (mean, SD)	VABS Social Standard Score (Mean, SD)	PLS-4 Expressive Communication Standard Score (Mean, SD)	PLS-4 Auditory Comprehension Standard Score (Mean, SD)	ADOS Severity Metric (Mean, SD)
M=305 F=60	38.21(8.48)	57.29(24.65)	72.24(9.02)	65.12(19.89)	69.78(17.13)	7.67(1.65)

TABLE 2: Baseline Model 1, Entire Sample

	Raw Scores Mean (SE)	**Standard Scores Mean (SE)**
Intercept Social Competence	25.00(0.41)*	72.31(0.48)*
Slope Social Competence	8.87(0.55)*	3.05(0.57)*
Intercept Language	26.79(0.61)*	65.09(1.08)*
Slope Language	11.04(0.67)*	9.50 (1.21)*
	Variance (SE)	
Intercept Social	43.78(5.87)*	65.20(8.30)*
Slope Social	42.99(10.81)*	78.77(14.14)*
Intercept Language	133.20(9.77)*	409.33(31.78)*
Slope Language	82.11(9.59)*	313.20(32.68)*

* Estimate significantly different from zero, $p < 0.01$

TABLE 3: Hypothesized Model 2, Entire Group

	Unstandardized Regression Coefficient (SE)	**Standardized Regression Coefficient**
Intercept Social Competence – Intercept Language	1.33(0.16) **	0.76(0.06)**
Intercept Social Competence – Slope Social Competence	-0.28(0.33), p=0.39	-0.29(0.35), p=0.42
Intercept Language – Slope Social Competence	0.22(0.15), p=0.14	0.39(0.28), p=0.17
Intercept Social Competence – Slope Language	0.74(0.31) *	0.62(0.25) *
Slope Social Competence – Slope Language	0.64(0.22)**	0.50(0.15) **
Intercept Language – Slope Language	-0.34(0.15) *	-0.49(0.20) *
	Residual Variance (SE)	
Intercept Social Competence	43.74(5.9)**	
Intercept Language	56.44(11.09) **	
Slope Social Competence	39.52(9.05)**	

Slope Language	44.51(11.86)**			
Fit of Hypothesized Model	**χ2, 8 df**	**CFI**	**TLI**	**RMSEA**
Imputation #1	32.08, p<0.01	0.99	0.98	0.08
Imputation #2	20.82, p<0.01	0.99	0.99	0.07
Imputation #3	26.44, p<0.01	0.99	0.98	0.08
Imputation #4	29.81, p<0.01	0.99	0.98	0.09
Imputation #5	18.40, p=0.02	0.99	0.99	0.06

TABLE 4: Comparison of Intercepts and Slopes for Social Competence and Language, Lower- versus Higher Cognitive Score Groups

	Lower Cognitive Score Group (< 70 SS)	Higher Cognitive Score Group (70 + SS)
Mean		
Intercept SC	22.83(0.41)	30.82(0.77)*
Slope SC	8.45(0.57)	9.99(1.27)
Intercept LANG	22.09(0.46)	39.37(1.16)*
Slope LANG	10.22(0.68)	13.23(1.50) *
Variance		
Intercept SC	27.30(5.58)	40.95(11.87)
Slope SC	39.10(11.71)	49.98(22.00)
Intercept LANG	54.43(5.01)	126.33(18.33)*
Slope LANG	80.37(10.05)	79.29(18.04)

SC = Social Competence (raw VABS IR scores)

LANG= Language Ability (raw PLS4 AC scores)

* significant group difference according to $\chi 2$ difference test, $p < 0.05$

TABLE 5: Covariates in Predicting Variance in Intercepts and Slopes for Social Competence and Language Ability

Covariate	**Social Competence Unstandardized Regression Coefficients (SE)**		**Language Unstandardized Regression Coefficients (SE)**	
	Intercept	**Slope**	**Intercept**	**Slope**
Child Gender	-0.05(1.08) p=0.97	1.53(1.40) p=0.28	-0.44(1.33) P=0.74	-1.58(1.88) P=1.42
ADOS Severity Metric	-0.42(0.24) p=0.08	-0.40(0.30) p=0.18	-0.24(0.30) p=0.42	-0.32(0.31) P=0.35
ABC Irritability	-0.03(0.05) p=0.55	0.01 (0.07) p=0.87	0.18(0.06) p<0.01	-0.02(0.07) P=0.08
ABC Lethargy & Social Withdrawal	-0.27(0.05) P<0.01	-0.07(0.12) P=0.97	0.17(0.08) P=0.05	0.01(0.08) P=0.91
ABC Stereotypy	-0.33(0.10) p<0.01	-0.07(0.12) P=0.54	0.11(0.12) P=0.36	-0.27(0.15) P=0.08
ABC Hyperactivity	-0.08(0.04) P=0.04	-0.03(0.07) P=0.62	0.15(0.06) P=0.01	-0.06(0.07) P=0.35
Primary Caregiver Highest Level of Education	0.11(0.14) P=0.45	0.34(0.17) P=0.05	0.35(0.19) P=0.06	0.24(0.18) P=0.17
Household Income	0.33(0.14) P=0.02	0.10(0.18) P=0.58	0.01(0.18) P=0.95	0.18(0.17) P=0.30

Figure 1: Hypothesized Model 2.

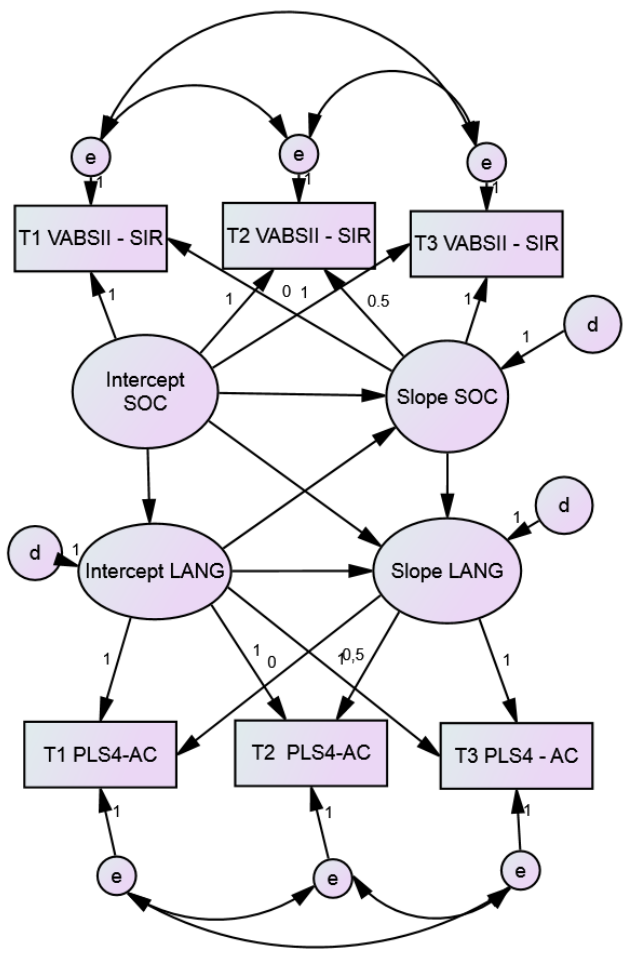
One-headed arrows depict regression weights/factor loadings.

VABSsirw = Vineland Interpersonal Relationships Subscale (Observed Score)

PLSacrw= Preschool Language Scale-4 AC Subdomain (Observed Score).

ICEPT lang = Intercept, Emerging Language Abilities

ICEPT soc= Intercept Social Competence



CHAPTER 5

CHAPTER 5

CONCLUSIONS

At the time when their child is first diagnosed with ASD, many parents describe similar anxieties: Will their child ever talk to them? Will he have friends? Will she live on her own? Parents tend to quickly learn firsthand and in lay terms what is meant by "heterogeneity in ASD" and the urgency of its real-world implications. Children with ASD are quite different from each other, and this difference has important implications for how they fare over time. Furthermore, such an understanding often fuels ever-increasing anxiety during the period between first concerns about their child and the time of assessment and, after diagnosis, while waiting for intervention. In a recent qualitative study, parents described their extreme feelings of urgency in accessing appropriate services, feeling there was an "optimal window" of time after diagnosis (Shepherd & Waddell, 2013. These important questions speak to the heterogeneity of ASD and, more specifically, to its *developmental* heterogeneity. Parents, caregivers, interventionists and others are less likely to be interested in how a given child with ASD compares cross-sectionally to other children at any one time, but how her/his presentation at time of diagnosis will predict how s/he will fare over time across multiple outcomes such as relationships, self-care, education and employment and emotional well-being. Understanding developmental trajectories in more complex ways is thus crucial to treatment planning.

Summary and Significance of Findings

The studies that make up this dissertation demonstrate how longitudinal cohort studies may incorporate theoretical frameworks from developmental neuroscience and cognitive psychology such as neuroconstructivism (Karmiloff-Smith, 1998, 2006; Sirois et al., 2008) and social orientation theory (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Dawson, Sterling, & Faja, 2010) to inform the clinical epidemiology of ASD. These are the first studies to investigate how two critical developmental domains -- social competence and language ability -- relate to each other over time in a representative inception cohort of children recently diagnosed with ASD. Such studies – theoretically driven, informed by developmental science and empirically tested by longitudinal studies -- are essential to understanding the complex developmental heterogeneity of ASD in as parsimonious and clinically relevant a manner as possible.

The studies in this dissertation address critical methodological gaps in the ASD literature to date. Early risk factor-outcomes studies in ASD involved small sample sizes (Eaves & Ho, 2008; Howlin, Goode, Hutton, & Rutter, 2004; Lotter, 1974; Sigman & McGovern, 2005) and only two time points (Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008; Eaves &

Ho, 2008; Howlin, Mawhood, & Rutter, 2000; Venter, Lord, & Schopler, 1992) and were therefore unable to capture heterogeneity and developmental change in children with ASD. Many studies also follow only children higher IQ (Szatmari et al., 2009) and lack an inception cohort (Cederlund, et al., 2008; Howlin, et al., 2004), thus increasing the likelihood of very biased samples. Finally, longitudinal studies that incorporate growth curve analyses have tended to analyse one phenotype or developmental domain at a time (Anderson et al., 2007; Anderson, Oti, Lord, & Welch, 2009) and so cannot depict a more dynamic and complex developmental picture of growth and change in children with ASD.

Many of the methodological constraints outlined in the literature to date limit, to varying extent, the internal validity and generalizability of their risk factor-outcomes findings. Most of these constraints limit our ability to infer whether developmental cascades may be part of the underlying developmental psychopathology of ASDs. Masten and Cichheti (2010) described the methodological requirements for strong tests of developmental cascade models of change: These include longitudinal data with repeated assessments of multiple domains or levels of function over time, as well as statistical approaches to analyzing complex models. More robust – and stringent – tests of cascade models should account for within-time covariance between developmental domains of interest and cross-time stability of each domain, to ensure that associations found are unique to specific variables and time points (Masten & Cicchetti, 2010). Finally, even the most stringent models cannot prove causality; however, testing the model in comparison to alternative models strengthens the robustness of findings -- e.g. by holding “cascade” associations to zero, changing specific paths or adding competing explanatory variables.

As demonstrated in this dissertation, specific patterns of cascades depend upon the underlying theory and hypotheses to be tested. More commonly, reciprocal cascades (also called “reciprocal effects models”) as outlined in Study #2 may be applied to developmental theories of skill-building by reciprocal scaffolding or “bootstrapping”: the attainment of skills within one domain scaffolds, or enables, learning in another which then in turn supports further improvement in the first. The cross-lagged auto-regressive model outlined in Study #2 provides such an example, incorporates within-time covariation between social competence and language, tests for cross-domain reciprocal effects while controlling for stability of each domain over time and may be compared to competing models (e.g. “no cross-domain effects”, “effects stronger in certain directions”).

Study #3 provides an example of a “feed-forward” cascade model in which reciprocal effects are not tested as much as “spillover” effects occur as advantages (or constraints) in one domain are associated with later growth in another. Dual- (or more) domain latent growth curve modeling enables the simultaneous modeling of variability and growth in each domain while testing for the effects from one parameter of growth of a given domain on the other. The addition of other domains and later time points can test for wider feed-forward spreading of effects from an upstream advantage or constraint across growth in multiple others, again testing against competing models.

Other cascade models, not tested in these studies, include mediation patterns and mechanisms of change in randomized controlled trials. Mediation models involve cascades of hypothesized effects across three or more developmental domains: Advantages in domain “a” lead to changes in mediator “m”, leading to changes in domain “b”. Using SEM, mediation models may be tested against models in which such patterns do not occur. Finally, the most robust test of developmental cascades would involve randomizing children with ASD to one intervention vs. a control treatment, in which the intervention aims to affect a critical domain in the cascade pathway. Subsequent investigation of the effects of treatment-related changes in a given domain (if any) on downstream pathways would then be compared to a control intervention which did not have such effects. To illustrate, one could hypothesize that an early intervention targeting social competence among very young children at risk of ASD may have wider-spread effects across multiple pathways than an intervention targeting a different developmental domain, such as language ability.

The studies outlined next describe results from the reciprocal and feed-forward cascade models tested in this dissertation, with an ensuing discussion of potential future steps in investigating developmental cascades in ASD.

Study 1

The first study set the foundation for the following chapters by demonstrating the importance of sound measurement of developmental constructs in longitudinal cohort studies. Although emerging social competence and language are strongly associated at the time of diagnosis, they may be measured as distinct developmental constructs. I was therefore able to confirm that in using these measures in children with ASD aged 2-4, one is not measuring cognitive abilities or behaviors that are fundamentally the same. This is particularly important to studies of developmental cascades and also to intervention studies that aim to detect spillover effects across multiple related outcomes. The distinctiveness of language from social competence is also important to large-scale cross-sectional genetic studies of children with ASD that aim to clarify endophenotypes involving cognitive or skill domains within the same “level” of the child. For example, language disability is an important co-morbid phenotype that may reflect an added genetic, or epigenetic “hit” in a “multiple-hits” model of ASD (Happe, 2003). In order to investigate this type of hypothesis, it is important to discern whether language ability is measurably distinct from core ASD impairments such as social competence. To our knowledge, this study is the first of its kind to do so in very young children with ASD using psychometrically sound measures of social competence and language aptitude.

Study 2

This series of studies was the also the first to convey a more dynamic picture of how children with ASD develop socially and linguistically after their diagnosis, using longitudinal latent analyses such as cross-lagged panels and dual-growth curve models. As shown in the second study, social and language abilities were highly stable in these young children. Contrary to our hypothesis, the reciprocal effects between social competence and language were relatively small: Children with ASD -- including those who were more cognitively able – did not demonstrate, to any large extent, a reciprocal pattern of development in which levels of social competence appears to scaffold language ability six months later, at least during the time frame and time lags chosen for our study. Instead, the cross-lagged panel design was valuable in demonstrating a pattern of developmental “uncoupling” of social competence and language during the time after diagnosis, as these domains became less strongly correlated, and possibly more specialized, over time.

Study 3

The third study built upon the second by describing the variability and the magnitude of change of the “specialist” social competence and language pathways. As such, the two cascade models may be viewed as complimentary. The previous study demonstrated the high stability of social- and language development during the year after a diagnosis of ASD in young children. However, the auto-regressive cross-lagged model that was developed could not describe variability and growth in these domains among children. Therefore, having established that reciprocal effects (which require an auto-regressive latent variable approach) were minimal, the latent growth curve analysis in chapter 3 enabled me to describe in a more nuanced way the highly stable “specialist” social and language pathways, and the extent to which initial levels and change in one domain influenced change in the other. The results of both studies are, in a sense, different – but equally and simultaneously valid -- snapshots of social and language development in very young children with ASD during the year after diagnosis.

The analyses in chapter 3 tested a “feed-forward” cross-domain model in which baseline advantages in one domain, particularly in social competence, were hypothesized to spill over to influence growth in the other domain. The results supported a social-orientation hypothesis: There was significant variability in social competence and language ability at the time of diagnosis, as well as in rates of change in the following year among preschool-aged children with ASD. A child's level of social competence at time of diagnosis and the subsequent rate of change in this domain were moderately-to strongly associated with improvements in language ability. However the converse association was not supported (in this sample and model) – baseline language ability did not appear to be a significant predictor of gains in social competence as measured by growth over the following year.

Notably, the results indicated that significant growth occurs in social competence and especially in language ability in the year after diagnosis, in fact outpacing the rate of improvement that would be expected in a normative sample of typically developing children. Furthermore, preschoolers with ASD who had cognitive scores within "normal" range outpaced their ASD peers within the sample with respect to language, but not social competence, gains. More cognitively able children also demonstrated stronger associations between social competence and language ability at time of diagnosis compared to less able children but showed relatively few differences in cascade patterns after diagnosis. Finally, as in studies of typically developing children (Gershoof, Aber, Raver & Lennon, 2007; Hoff & Tian, 2005; Perkins, Finegood & Swain, 2013), child- and family-level variables such as child behaviors, and indicators of family socioeconomic status (e.g. level of parental education, family income) were associated with individual differences in social and language development among young children with ASD

Implications

Developmental Cascades in ASD.

Do developmental cascades occur in preschoolers with ASD? According to the results of these studies they do, but in a particular pattern during a particular developmental period. Reciprocal cascade effects between social competence and language skills from time of diagnosis in young children with ASD appear to be very small, however "feed-forward" spillover effects occur from baseline social competence to language growth. This supports examples proposed by Masten and Cicchetti in which gains in one developmental domain may spread across other domains or levels (Masten & Cicchetti, 2010). The cross-domain associations were stronger at the time of diagnosis and became evident once rate of change was taken into account for social competence and language ability. Although such correlational results cannot confirm causation, these findings support Dawson's social orientation theory that early social competence skills vary between children with ASD, and that early strengths therein may facilitate the rate of language development in the year after diagnosis.

Second, the results of the second and third studies remind us that whether or not cascades occur depends on *when* you measure them. This set of studies followed preschoolers with ASD after the time of their diagnosis, which was shown to be an important period for social- and language development. However, there were indications that cross-domain interactions may occur prior to this relatively short time frame: Baseline correlations between social competence and language were stronger, and as demonstrated in Study #2, became weaker over time. Furthermore, among clinical subgroups in these studies, children with ASD aged 2-4 years old who had “normal-range” cognitive scores also appear to have had more optimal developmental trajectories pre-diagnosis: by baseline of the study, they demonstrated significantly greater social and language skills, as measured, than their less cognitively able peers. It is possible that stronger cross-domain coupling between social competence and language occurs prior to diagnosis of an ASD during a period when such cross-domain effects typically occur in non-developmentally disabled children – the early period of great gains in joint attention and nonverbal communication followed by growth in word learning (Nelson, 2007). One hypothesis stemming from Studies #2 and #3 is that earlier cross-domain cascades (e.g. prior to age 2) may be stronger and proffer relative developmental advantages to cognitively higher-functioning children with ASD, at the start of a period when social competence and language pathways then begin to build on themselves. Alternatively, a third factor such as nonverbal IQ itself may account for the stronger baseline cross-domain correlation.

Why does a developmental cascade framework matter to ASD research? First, it demonstrates how the risk-outcome models and methodology of large-scale longitudinal studies of children may be applied to the study of developmental domains. Such an approach has great potential to inform our understanding of the unfolding developmental psychopathology of ASD, by providing empirical support from an epidemiological perspective for findings from experimental neuroscience research. For example, the progressive "uncoupling" of social competence and language ability in children with ASD aged 2-4 years old described by Study #2's cross-lagged model appears to support – at the level of cognition and behaviour -- Johnson's neurodevelopmental theory of interactive-specialization (Johnson & Munakata, 2005; Johnson, Grossmann, & Kadosh, 2009). According to this model, in typically developing children social and language functions may be more interdependent and less functionally distinct early in development, but as the child develops, brain regions and responses become more fine-tuned and specialized over time (Johnson, 2007). Early genetic, epigenetic or and/or neural deficits may be the rate-limiting step upstream in development that delays or constrains multiple growth trajectories of children with ASD; however, children with ASD may be more like, then different from, typically developing children with respect to unfolding patterns of developmental interactions between social and language pathways. These findings are very preliminary, however, and will require replication studies with control groups of typically developing children for further substantiation.

Clinical Implications of Cascades in ASD.

The results of these studies have important clinical implications. First, this research found that social competence is an important predictor of language growth in preschoolers with ASD, whereas the converse was not evident – language ability at time of diagnosis did not appear to influence social competence growth, as measured in this sample. Within Canada, publicly funded interventions vary widely by province and currently evidence-based early interventions (like the Dawson's Denver Early Head Start model or Kasari's joint-attention and play-based interventions) that target emerging social competence are rarely offered (Dawson et al., 2010; Kasari, Gulsrud, Freeman, Paparella, & Hellemann, 2012). In the province of Ontario, most of the intensive behavioural intervention programmes offered focus on early IQ and language abilities. This study provides important empirical support for interventionists' arguments that early social competence interventions should be considered an essential component in a range of treatments available to children at time of diagnosis with ASD (Dawson & Burner, 2011; Dawson & Zanolli, 2003).

Language interventions continue to be an important component of intervention and should be tailored to children with specific comorbid language impairment, possibly in addition to social competence services. It is possible (or perhaps likely) that language intervention may have cascading effects later in childhood beyond the timeframe of the current study: Longitudinal follow-up studies may determine if intervening early on language impairment influences other domains (e.g. adaptive functioning, psychiatric co-morbidity) later during childhood. Furthermore, these results support a small but growing awareness of psychosocial constraints on the development of children with ASD (Anderson, et al., 2007). Interventions must address potential barriers to optimal uptake and outcomes such as family income, parental education, as well as children's emotional and behavioural co-morbidities.

A second implication considers the role of diagnosis as a gatekeeper to intervention. The suggestion that stronger reciprocal effects between early social competence and language abilities may take place prior to age of diagnosis supports arguments that social competence interventions should occur early – i.e. during the toddler years, when there is greatest potential for cross-domain and downstream effects (Dawson, Rogers, et al., 2010; Wallace & Rogers, 2010). Such interventions are currently aimed at high-risk groups of baby sibs of children with ASD, but could be offered to other high-risk children who demonstrate early social-communication delays for any reason – e.g. related to early environmental deprivation, to the cognitive profiles of genetic syndromes or emerging language disabilities and non-specific developmental delays (Howlin, et al., 2000; Mawhood, Howlin, & Rutter, 2000; Pollak, Cicchetti, Hornung, & Reed, 2000; Zadeh, Im-Bolter, & Cohen, 2007). Screening for delays in early social skills such as joint attention and social reciprocity, as occurs in some regions at 18 months at a population level, could then lead to targeted early intervention focusing on such skills while caregivers continue to monitor progress and families wait for a more focused diagnostic assessment (Mousmanis & Watson, 2008). Further research is needed into the early social-developmental prognostic markers of later mental health problems in children. Nevertheless, it is possible that early intervention for toddlers and preschoolers who will not go on to have ASD may benefit a wider range of children at risk of falling further behind. Waiting for a diagnosis of ASD to be made may miss out on an optimal intervention period when gains made in social competence may yield a greater array of improved outcomes.

Limitations

Several limitations must also be noted. First, the associations noted in these studies are correlational, and cannot prove causality.

Further studies from an epidemiological and neuroscience perspective will be important to replicate these results in different samples using different measures and approaches. The convergence of neuroscience, longitudinal/observational and intervention research findings would further support the theory of developmental cascades as causal mechanisms in ASD. Second, due to a lack of measures available, it was not possible to include multiple informants and methods in this study. Because parents respond to the PLS-4 when children are pre-verbal, and to the VABS-II in interview format, there is a risk of shared method and/or informant bias. The possibility of significantly biased correlational findings appears to be less concerning given that the variables for social and language competence were more strongly correlated among older and higher-functioning children (who would be tested more directly by psychometrists on the PLS-4). Third, as detailed in Study #1, multiple imputation strategies attempted to account for children who had to change language measures after reaching ceiling levels on the PLS-4; nevertheless the data may be somewhat skewed towards linguistically lower-functioning scores as a result. Fourth, due to power and sample size issues in such complex models, I was unable to adjust the associations in the models for a number of covariates. Finally, I included an index of nonverbal IQ (cognitive score) as a categorical moderating variable (“normal”-range vs. lower scores) rather than as a continuous covariate, because such cutpoints are often used in clinical services. However, this may have prevented a more fine-grained analysis of the effects of cognitive ability on social competence and language development. Future studies may address these issues.

Perhaps most importantly, the relatively small number of time points available for this study limits the extent to which we can generalize the occurrence of cascade patterns in developmental time. Reciprocal cascades may occur during a different developmental window, such as prior to diagnosis, or across a longer span of time than 6-months or 1 year. For example, social competence at age 2 may predict language ability at age 6, which in turn may predict the delayed acquisition of theory of mind at age 12, the latter of which associations has been found another study (Bennett et al., 2013). The arbitrariness and inflexibility of time points based on chronological age is often a practical necessity in large longitudinal cohort studies that recruit children based on age at diagnosis and which must also consider response burden (and subsequent participant attrition) in deciding upon an optimal assessment schedule. An obvious limitation of longitudinal research is the time investment required to wait for participants, and thus the data, to “grow up”. In the case of this study, further data from the Pathways Study will become available in the near future, enabling the extension of these models into latent childhood.

Such trade-offs occur in using large epidemiology datasets to investigate developmental questions: Although developmental epidemiology researchers can attempt to capture developmental *windows* – time frames when important developmental milestones are likely to occur in a typically-developing or disabled population --, one cannot generally catch developmental *thresholds* – the point at which a child moves from absence to acquisition of a particular ability or interest. The ability to capture such thresholds more accurately is a strength of other methodologies in developmental neuroscience. This speaks to the need for an iterative body of developmental research literature that addresses similar questions using complementary study designs and samples.

Beyond the limitations of the current studies, several broader caveats should be noted about potential hazards of translational research bridging the disciplines of cognitive or developmental neuroscience and epidemiology. First, drawing upon theory and findings from one body of knowledge to guide research in another requires equally strong critical appraisal of both fields. Second, care must be taken to avoid "naming fallacies" in drawing conclusions about child development in epidemiology studies, particularly when latent variables are developed to represent particular constructs. Saying that a certain model represents a given developmental phenomenon does not make it so, particularly when inferences are made about neural or cognitive processes based upon data measured at the level of child behaviour. Conclusions should only be drawn about developmental processes at the behavioural level, but may inform or guide further research at more "micro-" level (e.g. experimental paradigms, functional neuroimaging).

Finally, developmental neuroscience and epidemiology researchers must always be clear about the representativeness of the group of children they are studying, and how elements of study design beyond recruitment and sampling may influence this. Even epidemiology studies that incorporate gold standard methods to sample populations of children with ASD, including the use of inception cohorts, will fail to give a "true" representation of all children with the disorder if behavioural measures employed cannot capture the true abilities of all participants – e.g. children who are unable to complete the task due to severe intellectual disability or challenging behaviours, or those who are too competent on a given measure to obtain a ceiling level. Furthermore, longitudinal studies offer little benefit over cross-sectional research if measurement problems such as floor/ceiling effects or a lack of measurement invariance distort the developmental picture. Such hazards emphasize that an enthusiasm for cross-disciplinary developmental science research between the levels of the brain/cognition and child behaviours/populations must not supersede the methodological rigor required of each field. Furthermore, they highlight the importance of truly interdisciplinary centres and teams whose members – from geneticists to epidemiologists to interventionists to parent advocates – inform, collaborate and challenge each other.

Future Studies

The studies described here would benefit from replication and elaboration of the concept of developmental cascade models. First, the findings reported in this study would benefit from a comparison with developmental patterns in non-ASD children. Do children with ASD differ from typically developing children and non-ASD children with language impairment with respect to more complex developmental patterns involving social and language development? Do children with ASD who progress more rapidly with respect to social-communication skills differ from those who do not with respect to such patterns? For example, “developmental coupling” between IQ and language -- associations between ability in one domain and growth in the other -- was studied in children with and without dyslexia (Ferrer et al., 2007). Researchers found that children with dyslexia who were able to compensate for their disabilities demonstrated patterns of stronger developmental coupling compared to children with dyslexia who could not catch up with respect to reading, but the IQ-language relationships were strongest for typically developing children (Ferrer, et al., 2007). Such an association may differentiate children with ASD who experience more optimal outcomes from those who show less developmental progress. Understanding the extent to which developmental cascade or compensatory patterns are specific to ASD would improve our understanding of its developmental psychopathology and provide longitudinal evidence for theories that could then be tested using more detailed analyses like functional brain imaging. It can also identify at-risk groups and help to further customize intervention strategies.

Future studies should test for cascade effects between a larger number of developmental trajectories, incorporate a wider range of developmental methodology approaches and cover a longer time period than was possible in these studies. Since early language ability has been shown to be a strong prognostic indicator of multiple outcomes, cascade models should test hypotheses about the role of language development as a possible mediator between early social competence and other outcomes, such as emotional and behaviour problems or educational attainment in children and adolescents with ASD. Other longitudinal analytic approaches may further refine our understanding of the nature of developmental cascades and whether they differ between children with ASD. For example, while I used an arbitrary, albeit clinically relevant, cut-off of 70 standard score points on a cognitive score to compare patterns between children, more person-centered analyses could identify groups of children who differ by the shape of particular developmental trajectories – e.g. children who make progress over time with respect to ASD symptoms or functioning, compared to others who plateau or regress. Statistically derived groups (e.g. using growth mixture modeling or similar techniques) could be used to compare whether children with more optimal developmental pathways differ from those who do not progress as quickly with respect to differences in the nature and strength of cascade associations between important developmental domains.

Perhaps most importantly, longer time spans can capture developmental continuity and discontinuity in potential cascade patterns. These studies emphasize the importance of identifying *which* risk factors and processes may be highest-yield with respect to intervention (e.g. which have the greatest "downstream" effects across multiple outcomes) as well as *when* they may have greatest effect. Whilst costly, future studies need to extend farther back and forward in time in order to capture critical periods for developmental cascades. For example, intervening during the infant and toddler years, when early neuroimaging biomarkers may identify children at risk of ASD (e.g. atypical brain responses to social stimuli, Elsabbagh et al., 2012) may be particularly powerful; during the time prior to diagnosis focusing on emerging social competence may have stronger effects across multiple developmental domains prior to a later time when abilities become more specialized. By extension different patterns involving varied child- or context-level variables may become more apparent later in development, for example reciprocal developmental effects may be more likely to occur between a child's social competence and their peer environment during late childhood/adolescent years for more cognitively able children with ASD. Ideally, identifying developmental continuity and discontinuity in complex interactions between trajectories of change will help focus intervention on high-yield skills (or contexts) during periods of optimal response across multiple domains.

Conclusion

Children with ASD demonstrate significant growth in social competence and language in the year after diagnosis, although significant variability occurs with respect to baseline abilities and progress. Social competence and language ability are measurably distinct but strongly related at time of diagnosis, and in the ensuing year these abilities appear to become less tightly linked. However, relative advantages in social competence at time of diagnosis appear to spill over to influence language growth in very young children with ASD. The associations between early language and subsequent social development do not appear to be as strong. These findings highlight the importance of early interventions focusing on social competence. Future research should elaborate upon further cascading effects of social competence across other developmental pathways.

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