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# Facilitators of communication and the development of autism

*From responsiveness to basic communicative cues,  
to emerging pragmatic language use*

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### **Abstract**

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When we communicate with others, we use a variety of abilities to facilitate and enable that communication. These abilities range from being responsive to others' communicative cues to making one's own communication more functional. Such facilitators of communication has been suggested as atypical in the development of autism. Reduced infant responsiveness towards communicative cues — such as speech sounds and direct gaze — have been suggested as precursors of autism. Pragmatic language use — to use language in a functional way in social interaction — is considered a core aspect of the condition later in development.

In this thesis, I used diverse methodologies to study the association between these facilitators of communication and autism early in life, utilizing an infant sibling study design. In Study I, basic attentional responsivity to social and non-social sounds in infancy was tested using pupillometry. Responsivity to the non-social sounds, but not the social sounds, differentiated infants with and without subsequent autism. In Study II, infants' behavioural responsivity to others' direct gaze was tested in real-life interaction. Neither how much nor how quickly the infants looked towards the other person's face after the direct gaze was reliably linked to later autism. Lastly, in Study III, two-year-olds use of pragmatic language was assessed with caregiver-questionnaires. We found a specific association between emerging pragmatic language use and dimensional autism already this early in life.

The findings of this thesis suggest that infant responsivity to speech and direct gaze are not clear precursors of autism. Yet, the emerging ability to use pragmatic language seem to be linked to autism already by two years age. This thesis thus contributes to the understanding of early development of autism and how it relates to responsivity to, and use of facilitators of communication during the first years of life.

*Keywords:* Autism Spectrum Disorder; Communication; Auditory responsiveness; Direct gaze; Pragmatics; Pupillometry; Live eye tracking; Infant siblings; Developmental Psychology

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*To my family.*



# List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

- I. Rudling, M., Nyström, P., Bölte, S., & Falck-Ytter, T. (2022). Larger pupil dilation to nonsocial sounds in infants with subsequent autism diagnosis. *Journal of Child Psychology and Psychiatry*, 63(7), 793-801
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- III. Rudling, M., Portugal, A. M., Bölte, S., & Falck-Ytter, T. (2023). Pre-pragmatic language use in toddlerhood: Developmental antecedents, aetiological factors, and associations to autism. *JCPP Advances*

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Maja Rudling contributed in the following way to the three studies included in this thesis: Specified hypotheses and planned analyses (including analysis plans), pre-processed data and performed data analyses, had a major role in interpreting the results, and wrote the manuscripts in Study I, II and III. This work was done in collaboration with supervisors and co-authors with progressing independence. In Study III Maja Rudling also conceived the idea for the study.



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# Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
ADI-R	Autism Diagnostic Interview – Revised
ADOS-2	Autism Diagnostic Observation Schedule – Second Edition
ANOVA	Analysis of Variance
AOI	Area of Interest
ASD	Autism Spectrum Disorder
BAP	Broader Autistic Phenotype
BATSS	Babytwins Study Sweden
CSS	Calibrated Severity Scores
DSM-5	Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition
EASE	Early Autism Sweden
EEG	Electroencephalography
EL	Elevated Likelihood
EL-ASD	Elevated Likelihood with Subsequent Autism
EL-notASD	Elevated Likelihood Without Subsequent Autism
fNIRS	Functional Near Infrared Spectroscopy
IQ	Intelligence Quotient
MSEL	Mullen Scales of Early Learning
NVIQ / VIQ	Non-Verbal / Verbal Intelligence Quotient
RRB	Restrictive and Repetitive Behaviours
SA	Social Affect
TL	Typical Likelihood



# Introduction

*It is nine o'clock on a Sunday morning. A ten-month-old infant is sitting in a highchair by the table, playing with her breakfast. Next to her, her brother is joyfully eating his pancakes while talking about the circus show they went to yesterday. The clowns were his favourite part. Their father is by the sink, dishing up the frying pan with the tap running. Meanwhile, their mother is trying to draw the infant's attention to herself, by looking at her and talking with an infant-friendly tone of voice – the mother wants to know if she would like another piece of banana.*

In our daily life, we are constantly processing information from multiple sources: Sounds, taste, bodily feelings, smell, sight, tactile information. To sort, select, weigh and reject different aspects of this information flow is essential to not be overwhelmed but instead learn from the environment. Social communication pertains to the transferring of information between people. In the scene above the mother tries to communicate with the infant, and to do this, she seeks the gaze of the infant to establish eye contact and talks with a tone of voice intended to draw the infant's attention. Both function to make communication more likely to happen – to facilitate communication. In this thesis, *facilitators of communication* refer to aspects of the communication that are not directly related to the communicated message. Instead, these are aspects that functions to promote communication, for example by making communication more likely to occur and more functional once it does.

Depending on how the infant responds her mother's signals to facilitate the communication, the kitchen scene will turn into different kinds of learning opportunities. If the infant in the scene above has an attentional system that tends to be directed towards the communication facilitating cues of her mother, such as the direct gaze and the sound of her mother's voice, that breakfast scene turns into an opportunity to learn language, communication, and social interaction. For example, she might learn about the connection between the sound 'banana' and the sweet, mushy foodstuff that is so fun to smash into the table. Conversely, if the infant has an attentional system that tends to be directed towards the sound of the running water, the breakfast scene turns into an opportunity to learn about repetitive noise or other aspects of that sound, but not necessarily social learning. If the attention of the infant is instead

equally drawn to the sound of water and speech, she might feel overwhelmed by all the information and avoid looking towards her mother's eyes to not be flooded by even more information. Even small differences in basic attention may thus lead to different ways of perceiving the world and in turn into different learning opportunities. When repeated continuously throughout early development, two infants with initially small differences in how they respond to other's communicative cues may develop quite different ways of functioning, with potentially cascading effects on their whole cognitive system.

Further on, as children develop more advanced ways of communicating themselves, they also develop ways to facilitate their own communication. Pragmatics is the use of language in interaction. We use it to adapt what, when and how we communicate to the current social context. Pragmatics thus functions to make linguistic communication more functional, and can therefore be seen as a facilitator of communication. Therefore, while directing attention towards communicative sounds and responding to others' direct gaze are primarily ways of making communication more likely to occur, pragmatics is a way to make communication more functional once it does.

This thesis is about the association between facilitators of communication and the neurodevelopmental condition autism. In this introduction, I start by presenting autism: How it is defined and expressed, what we know about the causes, and theories of autism and autistic development. Then I move on to communication, and more specifically facilitators of communication. I focus on three aspects of facilitation of communication: Responsivity to speech and direct gaze, and emerging pragmatic language use. These aspects are presented both in terms of their suggested link to autism and in relation to the aims of this thesis. Next comes the methods section, followed by summaries of the three studies that make up this thesis; how they were made and what we found. Lastly, I will discuss the findings of the studies in relation to the aims of the thesis, and to theoretical and practical implications.

For the purposes of this thesis I will use identity-first language and the terms often preferred by people on the autism spectrum (Bury, Jellett, Spoor, & Hedley, 2020; Kenny et al., 2016). I will therefore use the terms *autistic* instead of *person with autism* or *person with ASD*. Infants who are not yet diagnosed will be referred to as *infants with subsequent autism* or *infants who later meet the diagnostic criteria*. However, for clarity's sake I will sometimes use the acronym ASD to refer to the diagnosis autism spectrum disorder as it is currently defined in DSM-5.

## Autism

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by atypical social communication and interaction, as well as restricted and repetitive behaviours. To receive a diagnosis, the current diagnostic manual by the American psychiatric association (DSM-5) states that one must have *persistent deficits* in social communication, social interaction and social reciprocity, such as difficulties in initiating and responding to social interactions, atypical eye contact and non-verbal communication, and difficulties with maintaining relationships. A diagnosis further requires restricted behavioural patterns such as stereotyped motor movements, insistence on sameness, restricted intense interests and/or sensory sensitivity, such as both hyper- and hyposensitivity, and sensory seeking. Symptoms of autism must have been present already in early development and lead to significant impairment of functioning (American Psychiatric Association, 2013).

Autism is pervasive, meaning that it colours many aspects of life. Apart from the social communicative and restricted behavioural aspects of ASD, autistic and non-autistic people have been shown to differ for example in regard to perception and sensory processing, emotional regulation, motor behaviour, and attention (Fournier, Hass, Naik, Lodha, & Cauraugh, 2010; Hanson et al., 2013; Rogers & Ozonoff, 2005; Zwaigenbaum, Bryson, & Garon, 2013). Autism is also a heterogeneous condition, both in terms of its' aetiology, manifestation and prognosis. This heterogeneity means that autism affect autistic people in individual ways, with variable levels autistic traits and patterns of strengths and liabilities associated to them. Although having autism is associated to negative long-term outcomes such as loneliness, limited independence and lower self-reported quality of life, the prognosis is contingent on both internal factors such as the pattern of how autism is expressed in each individual, and external factors such as access to environmental support (Barneveld, Swaab, Fagel, Van Engeland, & De Sonnevile, 2014; Lawson et al., 2020; D. Mason et al., 2018). Autism can also be associated to comparative strengths, including memory for details, visual pattern identification and visual search, pitch discrimination, early development of text decoding, and computational abilities (for reviews, see Happe, 1999, and Meilleur, Jelenic, & Mottron, 2015).

### The aetiology of autism

Autism is highly heritable (Colvert et al., 2015; Sandin et al., 2017). This means that someone who has a family member with an ASD diagnosis, are more likely than the general population to be autistic themselves (Hansen et al., 2019; Ozonoff et al., 2011; Sandin et al., 2014). For example, around 20% of siblings of children with an ASD diagnosis also meet the diagnostic criteria

(Ozonoff et al., 2011), compared to the prevalence of around 1-2% in the broader population (Idring et al., 2015; Szatmari et al., 2016). This likelihood increases the more autistic family members one has and the closer in relation you are (Sandin et al., 2014). Hundreds of individual genes have been linked to the condition, with a large number of genes each making a small contribution, and a small number of genes potentially making large contributions to the likelihood of autism (Betancur, 2011; Kiser, Rivero, & Lesch, 2015; Weiner et al., 2017). Importantly, even though autism is heritable, the genetic makeup does not in itself determine autistic outcome. Instead, heritability is likely driven by a combination of environmental aspects and genetically inherited traits, some of which are specific to autism and other's which are generally present in the broader population (Constantino, Charman, & Jones, 2021; Johnson, Charman, Pickles, & Jones, 2021; Jones, Gliga, Bedford, Charman, & Johnson, 2014; Kiser et al., 2015). As with the genetic factors, a large range of environmental factors contribute to the likelihood of autism (Catherine Lord et al., 2020). Thence, throughout development, the genetic and environmental factors interact in complex ways, altering brain development, and skewing the developmental path away from typical development (Constantino et al., 2021; Johnson et al., 2021; Kiser et al., 2015).

## A historical background of autism

Since Leo Kanner first described infantile autism eighty years ago (Kanner, 1943) the view of the condition has shifted over time. These conceptual shifts have reflected the current scientific and medical paradigms and understandings of typical and atypical functioning (Happé & Frith, 2020; Vivanti & Messinger, 2021). The initial definition of autism came to be in the context of a psychodynamic model of development, wherein the focus lay on the child's earliest relationships. Even though Kanner had suggested in his early writings that autism was biological in origin, throughout the 1960's and 70's autistic behaviour was thought to be caused by emotionally unresponsive 'refrigerator' moms, not providing the sensitive upbringing that children needed (reviewed in e.g. Hertz-Picciotto, Schmidt, & Krakowiak, 2018; Vivanti & Messinger, 2021). This model, which put the responsibility for autistic children's difficulties on their mothers, was later challenged by research on the biological heredity of autism (e.g. Folstein & Rutter, 1977). However, by then a prototype of autists as being aloof and unresponsive had already been established in the medical and general public's view. In the 1980's and 1990's, cognitive models that explained certain main aspects of the condition were developed as a contrast to the psychodynamic theories that came before (Vivanti & Messinger, 2021). These models focused on certain levels and explanations at a time, a *primary deficit*. Prominent among these cognitive, primary deficit theories of autism were Baron-Cohen's account of autism being mainly driven by impairments in theory of mind or understanding others

mental perspectives (Baron-Cohen, 1990) and Uta Frith's model of weak central coherence suggesting that autistic cognition is characterized by a focus on details rather than the whole (Frith & Happé, 1994).

## Autism as dimensional, and the neurodiversity approach

In the last 30 years, the concept of autism has shifted from being viewed as a distinct, discreet and easily identifiable condition to being viewed as heterogeneous, dimensional and complex (Happé & Frith, 2020; Vivanti & Messinger, 2021). Autism is also increasingly viewed as existing on a continuum between typical and atypical functioning, where autism represents the quantitative extreme of certain behaviours and traits (Happé & Frith, 2020; Thapar & Rutter, 2021). An important driver of this shift is that autistic traits have been found to be normally distributed in the general population, and thus seem to exist in different quantities also in people who do not reach the diagnostic threshold (Constantino & Todd, 2003; Rubenstein & Chawla, 2018; Wagner et al., 2019). This shift towards a dimensional view of autism has been accompanied by the neurodiversity approach. Based originally in a self-advocated movement calling for a refocus from autism as pathological and impaired functioning to viewing autism as a different but not deficient way of functioning (Dwyer, 2022), these *neurodiversity* approaches suggest that the makeup of our central nervous system varies naturally throughout the population, and that this is a source of strength for human culture. Neurodevelopmental conditions such as autism can thus be biological in nature, but the negative consequences of an autistic way of function occurs mainly in the meeting with an unaccommodating environment that is adapted rather for neurotypical functioning (Bölte, Lawson, Marschik, & Girdler, 2021; Dwyer, 2022).

## Two accounts of the developmental basis of autism

Two competing explanations for the basis of autistic development are currently debated in the field: The *social first* and the *domain general* accounts. The *social first* account claims that autism is caused by early disruptions in social brain networks. For example, the social motivation theory suggests that autism stems from a difference in the neural social reward system, resulting in less interest in social interaction and cooperation than non-autistic people (Chevallier, Kohls, Troiani, Brodtkin, & Schultz, 2012; Dawson et al., 2004). Another social first theory proposes that the starting point of autism lies in specifically social attention (Klin, Shultz, & Jones, 2015). Empirical support for basic difference in social functioning in autism include findings that autistic children orient less to biological motion (Klin, Lin, Gorrindo, Ramsay, & Jonas, 2009), speech sounds (Ceponiene et al., 2003; Klin, 1991), and others' eyes (Jones & Klin, 2013) than typically developing children. The competing *domain general* account claim instead that widespread atypicalities in early

brain function, with a focus on early sensory, perceptual, and attentional functioning, is the basis of autistic development. One example is the Bayesian model of autistic development, which suggests that autistic infants differ from their typically developing peers in regard to how they are learning from the environment, specifically when the sensory information contradicts the expectations (Cruys, Evers, Hallen, & Eylen, 2014; Pellicano & Burr, 2012). Empirical findings that support a domain-general account of autism include typical performance in social perception and processing tasks in infancy in autism, but atypical domain-general perceptual performance, such as multisensory processing (Falck-Ytter, Nyström, Gredebäck, Gliga, & Bölte, 2018), and spatial auditory attention (Soskey, Allen, & Bennetto, 2017). A recent study found that while neural gene-expression differences were present throughout the brain in autistic adults, the most pronounced difference was consistently found in areas designated to sensory, not social, processing, which also supports a domain-general account above a social specific account (Gandal et al., 2022).

### A dynamical systems perspective on autistic development

Reflecting the heterogeneity of the aetiology of autism, it has been difficult to establish a simple, linear developmental route to autism that is similar for everyone with the condition. Instead, likelihood of autism might be better seen as evolving through development, due to a complex interaction between biological, environmental, and behavioural characteristics of each individual (Elsabbagh, 2020; Johnson et al., 2021) This means that two individuals with the same initial inherited likelihood might have different developmental trajectories and end up with different outcomes, one with autism and one without. Such a dynamical systems approach assumes that to understand a concept, one cannot focus on specific aspects in lieu of the whole. In this view, autism should be regarded as emerging from a complex and continual interaction between different aspects of the child and its' environment. It is this interaction that drives development and determines the outcome (Ahn, Tewari, Poon, & Phillips, 2006; Vivanti & Messinger, 2021). From this perspective, the goal of research directed towards understanding the development of autism should be: 1. To identify early neural and behavioural markers that are antecedents of autism infancy, and 2. To identify modifying factors that come in later in development and interacts with the early stage factors (Constantino et al., 2021; Johnson et al., 2021). Autistic individuals can have different combination of initial markers as well as later moderators, which can help explain the heterogeneity of both aetiology and outcome. The early biobehavioural markers of autism are likely limited in number. An important step towards understanding autism, which might also lead to earlier identification and intervention, is to map and identify these early makers already during the first year of life, before autism is manifested (Constantino, 2021; Constantino et al., 2021).

## Infant sibling studies

One way of studying the earliest development of autism, that capitalizes on the heritability of the condition, is the prospective infant sibling study design. In this design, infant siblings of children with ASD diagnosis are followed from early development into childhood. Increasingly, participants are included if they have a first-degree family member with autism, either a full-sibling or a biological parent (but the study design are still commonly referred to as infant sibling designs). Due to the heritability of autism, these first-degree family members have *elevated likelihood* of developing autism themselves. When the infants reach an age when they can be reliably diagnosed, typically around age three, they undergo rigorous diagnostic evaluations. The researchers can then retroactively group the infant participants into three groups: EL-ASD, which includes infants with familial elevated likelihood of autism who themselves meet the diagnostic criteria at three years age; EL-notASD which includes infants with an elevated likelihood of autism who do *not* meet the diagnostic criteria at three years age; and TL, which constitutes a comparison group of infants without family history of autism, who do not meet diagnostic criteria at three years age and therefore are deemed to have typical likelihood of autism. Based on this grouping, it is possible to retroactively study if infants who later meet the diagnostic criteria for an ASD diagnosis differ from non-autistic infants already early in development. Apart from the categorical group-based analyses, it is also possible to study associations between different early measures and later dimensional autistic traits. In this way, the early development of autism can be studied also beyond the diagnosis. In infant sibling studies, the overarching goal is to understand the earliest development of autism, to better understand variability in development and to hopefully be able to identify infants at increased risk of later having problems related to autism, and potentially develop ways to support these individuals already early in life.

## The broader autistic phenotype

In autistic families, non-autistic family members often have elevated autistic traits even if they do not themselves reach the threshold of diagnosis (Messinger et al., 2013; Pickles et al., 2000; Rubenstein & Chawla, 2018). The development of this *broader autistic phenotype* (BAP) show similarities to autistic development, albeit often to a lesser degree, with general lower social responsiveness in terms of responding to their name (Nadig et al., 2007), responding to others initiations of joint attention (Nyström, Thorup, Bölte, & Falck-Ytter, 2019), social smiles (Nichols, Ibañez, Foss-Feig, & Stone, 2014), delayed development of language and communication (Roemer, 2021) and other social and cognitive characteristics associated with autism (Pisula & Ziegart-Sadowska, 2015). Like ASD, BAP has been found to be associated to

negative long-term consequences such as difficulty to retain friendships, feelings of loneliness, anxiety and depression in adulthood (for a review, see Jobe & Williams White, 2007). Infant sibling studies has the potential to increase understanding of this group, and help us identify who are at risk of having negative consequences of the broader autistic phenotype already in infancy, with potential for directed support to alleviate that risk.

Furthermore, due to genetic overlap between several neurodevelopmental conditions, the genetic factors that increase likelihood of autism also increase the likelihood of conditions like attention deficit / hyperactivity disorder (ADHD), developmental language disorder, general learning disability, schizophrenia and depression (Anttila et al., 2018; Doshi-Velez, Ge, & Kohane, 2014; Jones et al., 2014; Messinger et al., 2013; Ozonoff et al., 2011). These are also common co-occurring conditions to autism, together with sleep and eating disorders (Mannion & Leader, 2013; Matson & Goldin, 2013). Infant sibling studies thus also have the potential to increase understanding of commonalities and disparities in the development of neurodevelopmental conditions in general.

## Communication

In its most basic form, communication is the transmission of information between entities. The word stems from the Latin verb *communicare*, which means to make something common (Rosengren, 2012). This definition involves a multitude of different types of communication between different types of entities, transferred in different media. In this thesis the focus is on social communication between human beings. Social communication here refers to the act of transferring information between people to develop common meaning by way of signs and symbols.

Social communication is a dynamic, interactive process that involves a back-and-forth of both receiving and producing information. It can be divided into verbal and non-verbal aspects. Non-verbal social communication includes facial expressions, gestures, and intonation, whereas verbal social communication includes core and pragmatic aspects of language use (R. Landa, 2007). Core language is the use of form (grammar and phonology) and content (semantics) to convey linguistic meaning. Pragmatics, in turn, is the adaptation and interpretation of language in relation to prior knowledge and social context (Baird & Norbury, 2016; Norbury, 2014; Reindal et al., 2021). In contrast to core language, pragmatics is an aspect of language that cannot be reduced to linguistic codes (Scott-Phillips, 2017; D. Wilson & Sperber, 2002). Pragmatic language use includes conveying context, resolving linguistic ambiguities, identifying and repairing misunderstandings, using and understanding

figurative language, making inferences, establishing common ground between interlocutors, and generally adapting what is said and how it is said to the interlocutor's background knowledge, the current social situation, and communicative goals (Baird & Norbury, 2016; Matthews, Biney, & Abbot-Smith, 2018; Norbury, 2014; Reindal et al., 2021; Zufferey, 2016).

What constitutes typical versus atypical social communication is difficult to assess in a standardized way, and even more so in early development as the rate of development of different communicative abilities varies greatly between children (Fenson et al., 1994; Tager-flusberg et al., 2009). The 'correct' way of communicating depends on communicative goals, cultural norms, personal style, context and the relationship between interlocutors (Adams, 2002). This means that communicative assessment is dependent on the communication of both participants, meaning both the assessor and the assessed. While there are standardized tests of communication, including of pragmatics, these tend to rely on report from caregivers or teachers who can assess communication in everyday life ((R. J. Landa, 2005; Norbury, Nash, Baird, & Bishop, 2004).

## Facilitation of communication

When we interact with others we continually send and respond to signals that facilitate communication and make both the communication more likely to occur and more functional once it does. Such communicative facilitators are not necessarily connected to the concrete communicative content, the message that is being transferred, but are rather paralinguistic aspects of communication that functions to enable and promote communicative effectiveness. In the following sections, I will expand on the previous introduction to facilitators of communication.

One aspect of communicative facilitation is the use of communicative cues like touch, social sounds or direct gaze which functions to signal to others our intention to communicate (Kampe, Frith, & Frith, 2003; Senju & Csibra, 2008; D. Wilson & Sperber, 2002). Such cues of communicative intent alert us towards how, when and where communication will ensue. Other peoples' voices, especially when directed towards us, signals to us to attend to the speech signal and the information therein (Kemple, Speranza, & Hazen, 1992). Likewise, when other people look directly towards us, this signals to us to attend to their faces, both because of the communicative information we can get from facial expressions and others' direction of gaze, but also because direct gaze itself signals to us a communicative intent (Csibra & Gergely, 2006). Such fundamental signals of communication are salient to us. Already at birth we typically show a preference for faces, which is a source of communicative cues such as gaze and speech sounds (Johnson, Dziurawiec, Ellis, &

Morton, 1991). New-born infants typically prefer speech over similar types of sounds (Vouloumanos & Werker, 2007). Similarly, new-borns are able to identify others' direct gaze and preferentially orient towards it (Farroni, Csibra, Simion, & Johnson, 2002). In a study on 6-month-olds, Senju and Csibra found that infant gaze following was dependent on being preceded by direct gaze or infant-directed speech (Senju & Csibra, 2008). Even though later studies have questioned such a dependency on communicative cues for gaze following to occur this early in life (e.g. Gredebäck, Astor, & Fawcett, 2018), the findings of Senju and Csibra still underscores that communicative cues affect behaviour and communication already this early in life. Notably, while cues of communicative intent, like direct gaze and infant-directed speech, can function to facilitate communication, this is not necessarily the complete function of these behaviours. For example, it is possible to look towards someone else without the intention of communication. During the first year of life, infants get increasingly proficient in their *responses* to other's attentional, emotional and communicative cues (Jones et al., 2014). In tandem, they develop the ability to *produce* cues of communicative intent, such as communicative vocalizations and gestures (Bates & Dick, 2002; Begus & Southgate, 2012; Bourvis et al., 2018; O'Neill, 2007).

Another aspect of facilitating communication are ways of making communication more effective and functional once it occurs. This can be done by way of non-verbal communication such as gestures, intonation, and facial expressions, or in terms of linguistic communication as with pragmatics (R. Landa, 2007; R. J. Landa, 2005). As children develop more extensive means of communication, they also need more sophisticated ways of facilitating that communication, beyond communicative cues. Pragmatics could be regarded as an adaptive means of facilitating ones' own verbal communication (Zufferey, 2016). Examples of how we use pragmatics to facilitate communication are by conveying context to statements, establishing common ground between interlocutors, adapting the communication to reach certain results, and identifying and resolving misunderstandings.

## Facilitation of communication and autism

Atypical communication is a core feature of autism (American Psychiatric Association, 2013). Such atypical communication can take different forms for different people, in different stages of life, and in different situations. In this thesis the focus is on three aspects of facilitation of communication in relation to autism: In Study I the focus is on infant attentional responsivity to social and non-social sounds in autism, in Study II the focus is on infant behavioural responses to others direct gaze in autism, and in Study III the focus is on emerging pragmatic language use in association to autism. In the following sections comes brief backgrounds of each of these studies.

## Responsivity to social sounds and speech in autism

Atypical responsivity and processing of sounds is common in autism (Kern et al., 2006; O'Connor, 2012), and auditory processing has been an important arena for debates between social-first versus domain-general proponents of autistic development. On the one hand, in line with the social-first account, both autistic adults and children have repeatedly shown atypical attention and responsivity to specifically speech and social sounds (Baranek et al., 2013; Ceponiene et al., 2003; Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Gervais et al., 2004; Klin, 1991; Watson, Roberts, Baranek, Mandulak, & Dalton, 2012). On the other hand, in line with the domain-general account, more recent studies have found support for atypical processing of non-social sounds (Cui, Wang, Liu, & Zhang, 2017; Kolesnik et al., 2019; Lloyd-Fox et al., 2018; O'Connor, 2012; Schwartz, Shinn-Cunningham, & Tager-Flusberg, 2018), as well as general hyperresponsivity to sounds in autistic individuals (Baranek, David, Poe, Stone, & Watson, 2006; Clifford, Hudry, Elsabbagh, Charman, & Johnson, 2013; Watson, Patten, Baranek, Poe, & Boyd, 2011). However, only a few studies have investigated basic attention towards social sounds and speech in relation to autism in infancy, even though that area of research might give important insights into the role of early sensory processing and attention in autistic development. One such study used functional near infrared spectroscopy (fNIRS). They found that 4-6 months old infants with subsequent autism showed less activation in brain areas typically involved in social perception (left temporal regions) when listening to vocal sounds but more activation when listening to non-vocal sounds than typically developing infants. The level of activation also correlated with degree of caregiver-reported dimensional autism at three years (Lloyd-Fox et al., 2018). Although the result of that study should be regarded as preliminary, as few participants were included (only five infants with subsequent autism), the atypical cortical activation in response to voices and vocalisations could indicate that differences in regard to processing of these stimuli can be found already in infancy in autism.

Thus, when it comes to early attentional responsivity to social sounds in autism, two important questions remain unanswered. First, in order to better understand the role of auditory processing in autism, the question is whether atypical basic attentional responsivity to sounds is an early precursor of autistic development. Second, in relation to the social-first versus domain-general accounts of autistic development, does infants with subsequent autism show atypical attentional responsivity to auditory stimuli in general, or is it specific to social sounds?

## Behavioural responses to direct gaze and autism

Reduced eye contact and feelings of aversion towards mutual gaze are common expressions of autism (Kliemann, Dziobek, Hatri, Steimke, & Heekeren, 2010; Trevisan, Roberts, Lin, & Birmingham, 2017). “Marked impairment” in eye-to-eye gaze is even listed as a diagnostic criteria in DSM-5 (American Psychiatric Association, 2013). However, despite the prominence of atypical eye contact in autism it is unclear when it emerges and how it develops. The detection of, and responding to, others’ direct gaze towards oneself are basic aspects of establishing eye contact (Csibra & Gergely, 2006). Such direct-gaze processing has been hypothesised to be central in the development of atypical eye contact in autism, and potentially even other aspects of autistic development such as atypical joint attention and theory of mind (Klin et al., 2015; Nation & Penny, 2008; Senju & Johnson, 2009; Senju, Kikuchi, Hasegawa, Tojo, & Osanai, 2008; Von Dem Hagen, Stoyanova, Rowe, Baron-Cohen, & Calder, 2014). Yet, few studies have investigated atypical direct-gaze responses in infants in relation to autism, even though that might elucidate the potential role of direct-gaze processing in autistic development. In terms of neural responsivity to direct gaze in infancy, Elsabbagh and colleagues found that a small group of infants with subsequent autism did not differentiate between direct and averted gaze in dynamic, computer generated stimuli measured by EEG (Elsabbagh et al., 2012). However, in a very recent follow-up study by Tye and colleagues on a much larger sample, that group difference was not replicated. Instead, they found that although neural processing of direct gaze in infancy was not a strong predictor of autism when analysed alone, it contributed to a diffuse pattern of face processing atypicalities that, taken together, was predictive of autism (Tye et al., 2022). This finding suggests that how infants process direct gaze might be best seen as one factor out of many that together skew the developmental path towards autistic rather than non-autistic development. In regard to real-life behaviour, Nyström and colleagues (2017) instead utilized live eye tracking to measure infant responses to an adult’s direct gaze in a playful interaction. They found that infants with elevated familial likelihood of autism looked less at the adult’s face shortly after the adult directed their gaze towards the infant, compared to infants with typical autism likelihood. However, that study did not include information on dimensional or categorical autism outcome.

Two important questions therefore remain unanswered regarding infant responses to direct gaze and autistic development. First, in relation to the hypothesis of direct-gaze processing being an important factor in early autistic development, is atypical behavioural responses to direct gaze an early precursor of autism? Second, to better understand the developmental trajectories of direct-gaze responsiveness, does direct-gaze responses develop differently in infants with subsequent autism than in infant without subsequent autism?

## Emerging pragmatic language use and autism

Atypical pragmatic language use is practically universal in autism (Baird & Norbury, 2016; M. Miller et al., 2015; Tager-Flusberg, Paul, & Lord, 2005; A. C. Wilson & Bishop, 2021b). In contrast, core language ability (the core aspects of language such as vocabulary, grammar and phonology) vary greatly between autistic people (Kjelgaard & Tager-flusberg, 2001; Tager-Flusberg et al., 2005). For example, in a study of parent-rated pragmatic ability, Miller et al. (2015) found that three-year-olds with elevated familial likelihood of autism had significantly lower pragmatic scores than their typical-likelihood peers. Over 80% of the children who exhibited this kind of pragmatic delay or impairment did not exhibit any general language delay. That finding supports the view that there is a dissociation between pragmatic and core language ability, which is the object of theoretical debate within the field (Carston, 2002; A. C. Wilson & Bishop, 2019, 2021a).

Pragmatic ability in childhood has been shown to be associated with important social facets of life, such as peer acceptance and relations in childhood (Kemple et al., 1992; S. M. Murphy, Faulkner, & Farley, 2014) and forming and maintaining close social relationships in adulthood (Whitehouse, Watt, Line, & Bishop, 2009). Pragmatic difficulties has also been suggested as contributing to conduct issues in children (Donno, Parker, Gilmour, & Skuse, 2010; Helland, Lundervold, Heimann, & Posserud, 2014). Despite how common difficulties in pragmatic language use are in autism, and despite the importance of pragmatics in our everyday life (e.g. Murphy et al., 2014), the earliest development of pragmatic language use and how it relates to the development of autism is not well understood (Reindal et al., 2021; Whyte & Nelson, 2015). Several factors contribute to this. Pragmatic ability is notoriously difficult to measure in a valid way, partly due to the fact that what is considered “correct” pragmatic language use is dependent on situation, culture, and norms (Adams, 2002; Baltaxe & 'Sangiola, 1996; Matthews et al., 2018). The construct of pragmatics also involves several different aspects of social language use. In fact, the validity of pragmatics as a cohesive developmental construct has been questioned, and as a consequence it has been suggested that we focus on pragmatic sub-skills rather than global pragmatics (Matthews et al., 2018).

In regard to early development of pragmatic language use in relation to autism two important questions remain unanswered. First, linked to the theoretical debate on the relation between core and pragmatic language, how is early pragmatic language use related to infant core language and social communication? Second, since pragmatic language use is so strongly linked to autism later in development, how is early pragmatic language use associated to autism already in toddlerhood?

# Aims of the thesis

The overarching aim of this thesis was to investigate the association between early aspects of communicative facilitation and the development of autism. This was in turn divided into two specific aims:

1. To examine if infants' responses to others' communicative facilitators, more specifically pupillary responses to social auditory cues (Study I) and behavioural responses to others' direct gaze (Study II), are early precursors of autistic development.
2. To examine if young children's ability to facilitate their own communication, more specifically in the form of pragmatic language, is associated to autistic traits and familial likelihood of autism in toddlerhood (Study III).

Study I and Study II thus focused on infant dimensions of autism. In Study I, the aim was to investigate basal reactivity to auditory stimuli. This was measured using pupillometry, reflecting noradrenergic activity in the brain. In Study II, the aim was to investigate responses to others' direct-gaze, measured in a live eye tracking situation to capture naturalistic social interaction.

Study III shifted focus from responses to others' communicative facilitation in infancy onto the ability to facilitate one's own communication in toddlerhood. In this study, the aim was to investigate developmental antecedents and the aetiology of early pragmatic language use, as well as associations to autism. This was done by studying parents' ratings of their children's early pragmatic language use (measured as decontextualized language, described under Study III) in both the general population and in children with elevated likelihood of autism.

# Methods

## Participants

The participants in the three studies of this thesis were part of one of two longitudinal studies: The Early Autism Sweden study (EASE; Study I, II, and III) and the Babytwins Study Sweden (BATSS; Study III). Both the EASE and BATSS studies were approved by the Regional Ethical Board in Stockholm, Sweden and conducted in accordance with the 1964 Declaration of Helsinki. Informed consent was collected from all parents.

Participants in both the EASE and the BATSS samples were recruited from the greater Stockholm area. They comprised mainly of middle-class families with a relatively high parental educational level (see Table 1 for sample characteristics). Exclusion criteria for both studies were premature birth (prior to week 34 for BATSS, and week 36 for EASE), any known genetic syndrome associated to ASD, diagnosis of epilepsy or history of convulsions, any known condition likely to affect brain development, or any known meaningful and uncorrected hearing or visual impairment.

### The EASE sample

The EASE study was a longitudinal autism sibling study wherein children with first-degree family members with an ASD diagnosis were followed from infancy (5 months age) to early childhood (6 years age). These children had an older sibling or parent with an ASD diagnosis, which was confirmed through clinical interviews and medical records. Due to the heredity of autism, the infant siblings had a familial elevated likelihood of developing autism themselves (EL). The EL children were recruited via the EASE project's website, advertisements, and clinical units. As a comparison group, infant with no first-degree family members with an ASD diagnosis were recruited via the Uppsala Child and Babylab's recruitment data base, based on birth records, forming the typical likelihood group (TL). All participants in the EASE study had at least one older sibling.

The three studies of this thesis include partly different participants (**Table 1**). This is due to different inclusion criteria in the three studies (such as a minimum number of valid trials) but also that recruitment and data collection was

ongoing during the course of the three studies. This means that when Study II was made, more children than in Study I had reached an age when they had been to the 36-months visits and could be grouped based on ASD outcome.

### The BATSS sample

BATSS was a longitudinal twin study, wherein infant same-sex twins were followed from infancy (five months age) into toddlerhood (three years age). They were recruited via the national population registry in Sweden. The zygosity of the twins was estimated using DNA from saliva samples. In BATSS information on familial likelihood of autism was not recorded, and for the purposes of Study III, they are considered to represent the general population in terms of autism likelihood.

**Table 1.** Group Characteristics for Study I, II, and III - *M / SD*

<b>Study I - EASE</b>			
	<i>Typical Likelihood</i>	<i>Elevated Likelihood Not ASD</i>	<i>Elevated Likelihood ASD</i>
<i>Total N (girls)</i>	31 (14)	50 (30)	18 (8)
<i>Chronological Age (10 Months)</i>	310 / 14	313 / 13	309 / 7
<i>SES (5-point scale)</i>	4.6 / 1.0	4.2 / 1.2	3.8 / 1.4
<b>Study II - EASE</b>			
	<i>Typical Likelihood</i>	<i>Elevated Likelihood Not ASD</i>	<i>Elevated Likelihood ASD</i>
<i>N (girls)</i>	40 (21)	94 (47)	35 (13)
<i>Chronological Age (10 Months)</i>	309 / 15	312 / 14	313 / 18
<i>Chronological Age (14 Months)</i>	431 / 20	429 / 17	438 / 17
<i>Chronological Age (14 Months)</i>	561 / 29	556 / 17	557 / 15
<i>SES (4-point scale)</i>	3.4 / 0.7	3.2 / 0.8	3.1 / 0.8
<b>Study III – EASE and BATSS</b>			
	<i>Combined Typical Likelihood</i>	<i>EASE Elevated Likelihood</i>	
<i>N (girls)</i>	206 (104)	97 (45)	
<i>Chronological Age (14 Months)</i>	438 / 19	429 / 20	
<i>Chronological Age (24 Months)</i>	756 / 26	743 / 29	
<i>SES (4-point scale)</i>	3.3 / 0.7	3.2 / 0.9	

*Chronological Age is reported in days*

## General procedures and measures of Study I-III

### Procedures of the EASE study

In the EASE study, participating infants and their caregivers visited the Uppsala Child and Babylab for a full day visit at ages 10, 14 and 18 months. At these visits the infants participated in different experiments, developmental assessments, and observations. The caregivers participated in parental interviews, and in connection to the visits they filled in several parental report questionnaires. The testing day went on for approximately 4 to 5 hours, and ample pauses, including a longer lunch break, was given in a flexible way to accommodate the participants needs for feeding and sleeping. All tasks were adapted to infants, and were made to be fun and positive for the participating families (Achermann, Bölte, & Falck-Ytter, 2020). If the infants showed clear signs of distress during any particular tasks, these were postponed to a later attempt or abandoned completely. After each lab visit, the families received a gift voucher of 500 Swedish kronor (which converts to around 50 euro). At 24 months and 36 months age, the infants and their caregivers instead visited the clinical research centre KIND, at Karolinska Institute in Stockholm. At these visits they also participated in experiments, developmental assessments, and evaluations, and parents filled in parental report questionnaires. At the 36-months visit the participating children underwent a full diagnostic evaluation by experienced clinicians using gold standard instruments and procedures, and participants who met the diagnostic criteria received clinical diagnoses of ASD.

For Study I and II, which included participants only from the EASE sample, we utilized the diagnostic information to retroactively form three groups: The EL-ASD group which comprised of children with an elevated likelihood of autism who received an ASD diagnosis themselves; The EL-notASD group which comprised of children with an elevated likelihood of ASD but who did *not* receive a diagnosis; and the TL group who comprised of the typical likelihood comparison group. See **Table 1** for group characteristics. One participant with typical likelihood of developing autism was excluded from the studies due to receiving an ASD diagnosis at this 36-months evaluation. At this 36-months visit, children could also receive preliminary diagnoses of ADHD and developmental language disorder, utilized in Study II.

### Procedures of the BATSS study

In the BATSS study, participating infants and their caregivers visited the clinical research centre KIND at the Karolinska Institute at 5 months age. There, they participated in different experiments and assessments, and the caregivers were asked to fill in questionnaires and participate in interviews. The zygosity

of the twins was also assessed using saliva samples. At ages 14 and 24 months the caregivers filled in parental questionnaires online.

In study III the aim was to study pragmatic language both in the general population *and* in associations to likelihood to receive ASD diagnosis. We therefore included both the EASE and the BATSS samples. The typical likelihood group from EASE was combined with one twin from each twin pair in BATSS to form the combined typical likelihood group, representing children from the general population. Only one, random twin from each twin pair was included in this group due to high intercorrelation between twins. The elevated likelihood group from EASE was compared to the EASE typical likelihood group for analyses of ASD likelihood. To perform exploratory twin analyses, both twins from each twin pair in BATSS was included.

## Measures included in Study I-III

In study I and II we analysed experimental data collected at the 10-, 14-, and 18 months visits and diagnostic data and outcome at the 36 months visit within the EASE study. In study III we analysed parental report data from the 14- and 24 months visits from both the EASE and BATSS studies. Some developmental and diagnostic measures were included in several of the three studies. These are described in the subsequent sections.

### ADOS-2

The Autism Diagnostic Observation Schedule, Second Edition (ADOS-2; Lord et al., 2012) is a standardized instrument used to measure observed behaviours associated with social interaction, verbal and nonverbal communication, and restricted and repetitive behaviours. These behaviours are elicited during semi-structured play. Different modules are used depending on developmental level of the participant, and in this thesis, either the toddler module or module 2 were used. To compare scores across modules we utilized the calibrated severity scores (CSS). The observation results in three CSS: The Total score, and the Social Affect score (SA) and the Restricted and Repetitive Behaviour score (RRB). Higher scores on these scales suggest more ASD associated traits in the individual participant. In EASE the ADOS-2 was administered at the 24- and 36 months visits, and was used as one of the instruments in the diagnostic process at the 36-months visits in EASE. The ADOS CSS were used in all three studies as measures of dimensional autistic symptoms and traits.

## ADI-R

The Autism Diagnostic Interview-Revised (ADI-R; Rutter, LeCouteur, & Lord, 2003) is a semi-structured parental interview aimed to assess children's autism associated behaviours as reported by their caregiver. The questions cover language and communication, reciprocal social interaction, and restricted, repetitive and stereotypic behaviours and interests. After administration, the answers are recoded into diagnostic algorithm scores. Higher algorithm scores indicated more behaviours linked to autism and ASD. Like ADOS-2, ADI-R was used as a measure of dimensional autistic symptoms and traits in Study I and II, and it is likewise used as a basis for the diagnostic procedure at the 36-months visits in EASE.

## MSEL

The Mullen Scales of Early Learning AGS Edition (MSEL; Mullen, 1995) is an individually administered, standardized test used to assess developmental level of infants and pre-school aged children. The test is divided into five cognitive and motor subscales: visual reception, receptive language, expressive language, fine motor and gross motor. These subscales are in turn transformed into composite standardized scores, constituting the Early Learning Composite, which is used as a measure of general developmental level or IQ. The scales can also be presented as the two sub-scales; verbal developmental level (VIQ; the receptive language and expressive language scales combined) and non-verbal developmental level (NVIQ; visual reception and fine motor). Higher scores of either scale indicate a higher developmental level. The MSEL was administered at all visits in the EASE study, and at the 5-months visit in the BATSS study. The NVIQ score was used in Study I and Study III as a covariate.

## Analyses of Study I-III

The hypotheses and analysis plans for Study II and III were publicly pre-registered in the Open Science Framework repository (OSF) after data collection but before the start of any data processing or analysis of the data. These analysis plans were open to reviewer. The hypotheses and analysis plan for Study I was not publicly pre-registered, but instead recorded on the EASE study's internal repository. Analyses were performed using IBM SPSS (version 25 in Study I and version 27 in Study II and III; IBM Corp., Armonk, N.Y., USA) Jamovi version 2.2.5.0 (in Study II; The Jamovi Project, 2021), and the PROCESS tool (in Study III; Hayes, 2013). In study III, the secondary twin analyses, were performed using R Version 4.0.0 and the OpenMx package version 2.18.1 (Neale et al., 2016).

# Study I

## Background and aims

In study I we measured basic reactivity to sounds in infants with and without subsequent autism. We used pupillometry, which is a measure of a noradrenergic arousal system in the brain. The locus coeruleus norepinephrine system (LC-NE) is centered in the brainstem kernel of locus coeruleus which plays an important role in regulating sensory processing and attentional orienting (Bast, Poustka, & Freitag, 2018; Mather, Clewett, Sakaki, & Harley, 2016; Sara & Bouret, 2012). The aims were to 1) examine if infant reactivity to sounds, measured with pupillometry, was associated to later autism and ASD diagnosis, and 2) to investigate if the infants with later ASD reacted differently to the social or non-social sounds compared to infants without subsequent diagnosis. We studied primarily infants at 10 months age, but also analysed if pupil reactivity to sounds changed between 10 to 18 months age. Because the link between pupil dilation and real-life behaviour is not well established in infants we added an additional analysis of the short-term associations between pupil dilation in response to sounds and gaze behaviour.

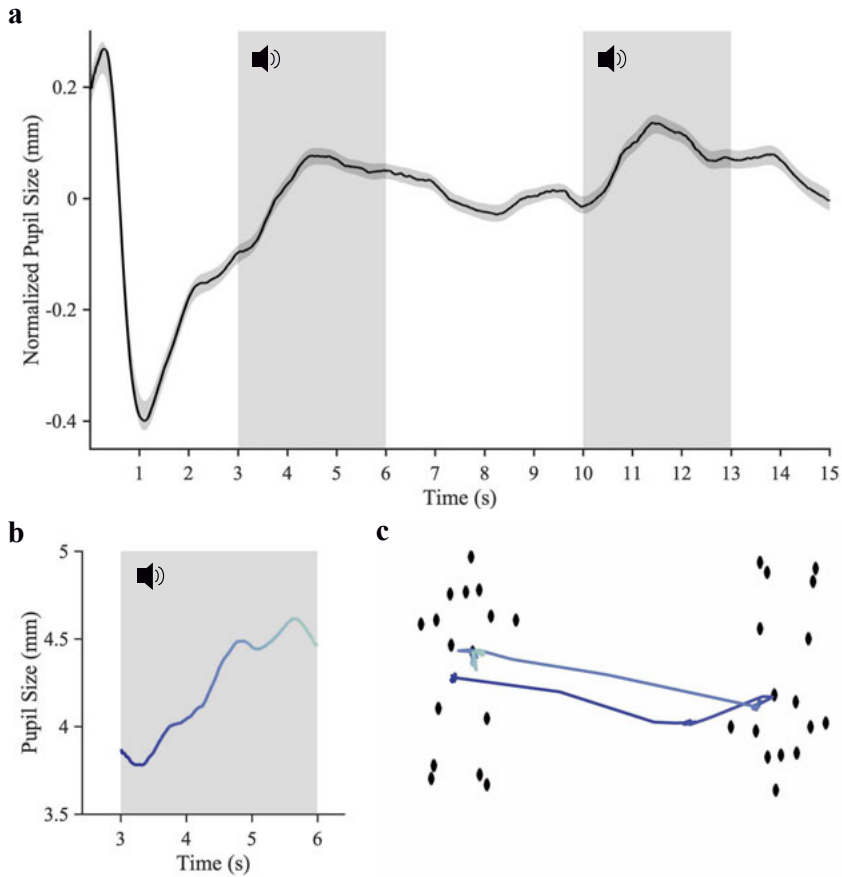
## Methods

### Experimental task

In study I we measured infants' pupillary responses to hearing two different types of sounds, which constituted the *Social Sound* and the *Non-Social Sound* conditions. The social sounds were the speech of two different women, speaking as if directed towards the infant and saying "hi sweetie, can you see me? Here I am!" in Swedish; The non-social sounds were the recording of water running from a tap. While listening to the sounds, the infants watched a video on the screen with two-point light displays of human movement, one inverted and one upright (**Figure 1, panel C**). This visual stimuli, which was also part of another experiment (Falck-Ytter et al., 2018), functioned as a visual attention grabber for the infants, making them focus their gaze towards the screen so the eye trackers could record their pupil.

The experiment was part of an approximately 10 minutes long screen-based eye tracking session, which also included experimental stimuli linked to other

hypotheses. The infants sat in their caregiver’s lap at circa 60 cm distance from a screen, on which the experimental stimuli were played, while an eye tracker recorded their gaze and pupils. This was done at the 10-, 14-, and 18 months visit to the lab.



**Figure 1.** An overview of the methods of Study I (data are normalized and smoothed): A) Mean pupil size across infants and both sound conditions. Grey rectangles represent the time periods when sounds were played during a trial (one social and one non-social sounds, counterbalanced across trials). Shaded area represents standard error of the mean. B) Pupil size for one participant when listening to one sound. C) The visual stimuli of biological motion. Gaze pattern of the same participant and trial as in B is overlaid in colour. Time is represented by colour with same time axis as in B.

## Measures and analyses

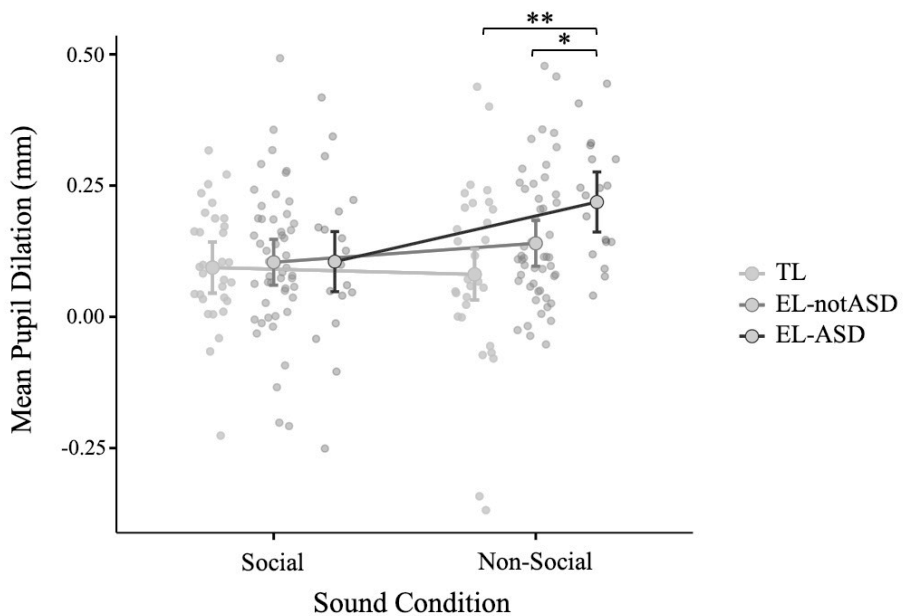
Pupil responses to the sounds were calculated as the difference between the pupil size (in millimetres) during a baseline period of 500 milliseconds before sound onset and the pupil size during the 3000 milliseconds that the sound was played. In the secondary analysis to investigate associations between pupil dilation and gaze behaviour, gaze shift frequency was operationalised as number of gaze shifts per second within a time window of 1000-5000 milliseconds after the sound onset. The threshold for counting a gaze shift was gaze movement velocity of 150 °/s.

The effect of group (EL-ASD, EL-notASD, and TL) on pupil responses to the two sound conditions were estimated using a repeated measures group \* condition ANOVA, followed by a simple effects analysis and Bonferroni corrected t-tests. Associations between pupil responses to the sounds and dimensional autism outcome were estimated using bivariate correlations between pupil dilation at 10 months (in the significant condition) ADOS-2 total CSS, ADOS-2 Social Affect, and ADOS-2 Restricted and Repetitive Behaviours as well as the summed algorithm scores of ADI-R. The association between pupil dilation responses and gaze behaviour was estimated by calculating individual regression coefficients with gaze shift frequency as the dependent variable and pupil dilation as independent variable across trials for each infant. The mean slope of these regression coefficients was then tested against 0 using a one-sample t-test. Effects of age was estimated using a linear mixed model with group (3), condition (2), and time point (3) as fixed effect factors.

## Results

In all three groups (EL-ASD, EL-notASD, and TL) the infants' pupils dilated as a response to listening to both types of sound (the social and non-social sound conditions). There was a significant interaction between group and condition (**Figure 2**), and when analysing the two sound conditions separately, the groups differed significantly from each other only in the Non-social sound condition. This sound elicited more pupil dilation for the infants who subsequently received an ASD diagnosis compared to both other groups. On an individual level, there was also a significant association between pupil dilation in response to the non-social sound condition at 10 months age and dimensional autistic traits at 36 months age, as measured with both ADOS-2 (including both subscales) and ADI-R. The analysis of a potential effect of age, which included data at the 10-, 14- and 18-months' time points, also showed a significant interaction between group and condition, and no significant effects including time point as a factor.

There was an association between pupillary reactivity to sounds and gaze behaviour on a short time scale, as more pupil dilation tended to be associated to fewer gaze shifts. This association did not differ significantly between groups. As a control analysis we tested if the groups differed in visual preference for the upright, biological motion, but found no significant group differences in looking time to the upright animation relative to looking time to the whole screen.



**Figure 2.** The mean pupil dilation in response to listening to the social and non-social sound conditions, between the three groups. Error bars represent 95%CI, \* $p < .05$ , \*\* $p < 0.01$ , Bonferroni corrected. Dots represent individual data points.

## Conclusions

The results of Study I suggest that infant reactivity to sounds is associated to both later ASD diagnosis and to dimensional autism in toddlerhood. The LC-NE system has been suggested to be involved in how the brain prioritizes and remembers some perceptual information over other (Mather et al., 2016) as well as in regulating attentional orienting to different stimuli (Bast et al., 2018; Sara & Bouret, 2012). Even small differences in sensory responsivity and basic attentional orienting early in life may have cascading effects on development more generally. Indeed, pupil dilation to the non-social sounds was associated both on short time scales with gaze behaviour, and on longer time scales with both social and behavioural dimensional aspects of autism. Our results thus suggests that basic sensory responsivity is a possible early marker of autism.

Contrary to our hypotheses, the groups differed only in regard to pupillary responsivity to the non-social sounds, which was the sound of running water from a tap, a quite repetitive noise. In contrast, the groups reacted similarly to each other in their pupillary responses to speech with a child-directed tone of voice. Because the two sound types are very different in semantic content and auditory aspects, it is difficult to know why they elicit such different responses in the infants with subsequent autism. However, taken together our results does not support a view that early sensory processing differences in autism is specifically social in nature. This conclusion is further underscored by the lack of group differences in visual preference for biological motion.

# Study II

## Background and aims

In Study II we measured how much and how quickly infants responded to the direct-gaze of an adult in a real-life interactive situation by looking back toward the adult's face. This study was a follow-up on the study by Nyström and colleagues from 2017, where they found that infants with typical and elevated likelihood of autism differed in how much they responded to others' direct gaze. The aims were 1) to investigate if behavioural responses to others' direct gaze in infancy was associated with subsequent ASD diagnosis and dimensional autism in toddlerhood, and 2) to study if the developmental trajectories of direct-gaze responses differed between infants with and without later ASD diagnosis.

## Methods

### Experimental task

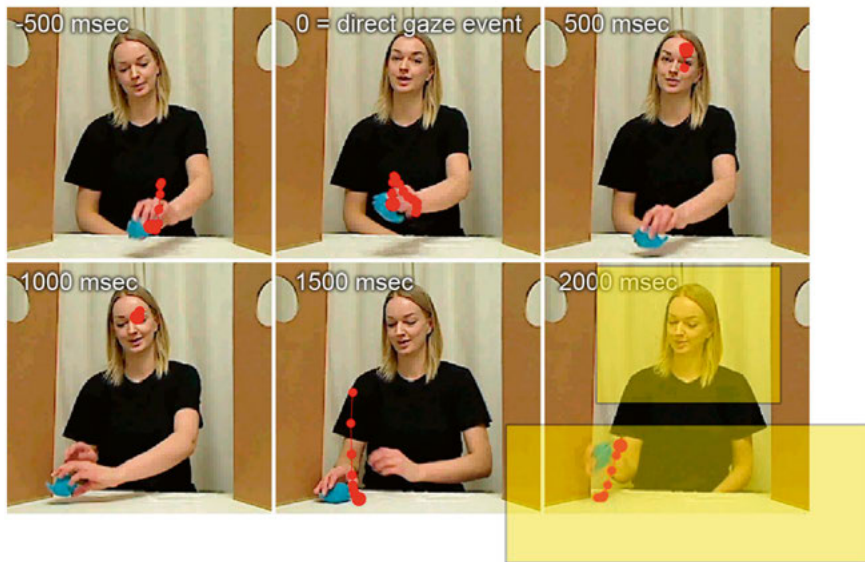
The infants participated in a live eye tracking session in which they sat in their parents laps circa 200 cm from a test leader who interacted with the infant from behind a low table. This approximately 10 to 15 minutes long live eye tracking session also included experimental tasks that were linked to other hypotheses. An eye tracker, placed between the infant and the test leader, recorded the infant's eye movements, while a scene camera recorded the test leader's behaviour, to enable mapping of the infant's gaze onto the real-life interactive situation they were watching. The caregivers were instructed to sit still and to not influence where the infant looked during the session. The infants participated in this session at the 10-, 14- and 18 months visits.

In the task analysed in study II, the test leader played with a small toy, moving it across the table and twice crashing it into a small wall. To draw the infant's attention to the action, the test leader made playful sounds and interacted with the infant in a relaxed and natural way. The test leaders gaze was predominantly averted from the infant, focusing on the toy in front of them. Intermittently, the test leader looked up towards the infant, seeking their gaze, as to share the experience with them. These initiations of eye contact constituted

the direct-gaze event. The task followed standard operating procedures, but because it was important that the interaction felt natural for the participating infant, each session was allowed to differ slightly in the timing and number of trials.

### Measures and analyses

The visual scene of the infant was divided into three areas of interest (AOI): The test-leader's face, the table with the toy, and the whole scene (**Figure 3**). *Face Preference* was defined as the amount of looking towards the face AOI divided by the amount of looking at the whole visual scene, which gave us a percentage of face looking preference.



**Figure 3.** An example of the visual scene of one infant in the direct-gaze interactive task. First, the test leader is playing with a toy, and then she looks up towards the infant constituting the direct gaze event and point zero in the trials. The participant's gaze data is super imposed in red dots. Yellow boxes represent the uncropped face and table/toy AOIs respectively. Used with permission from Nyström et al., 2017.

To measure overall change in amount of looking towards the adult's face after the direct gaze, the mean baseline value of Face Preference (500-0 milliseconds before the direct-gaze event) was subtracted from each 100-millisecond time bin of the measurement window (0-2000 milliseconds after the direct gaze event) giving us a value of change from before to after the direct gaze event:  $\Delta$  *Face Preference*. This was then averaged across a time window of 300-1000 milliseconds after the direct gaze event.

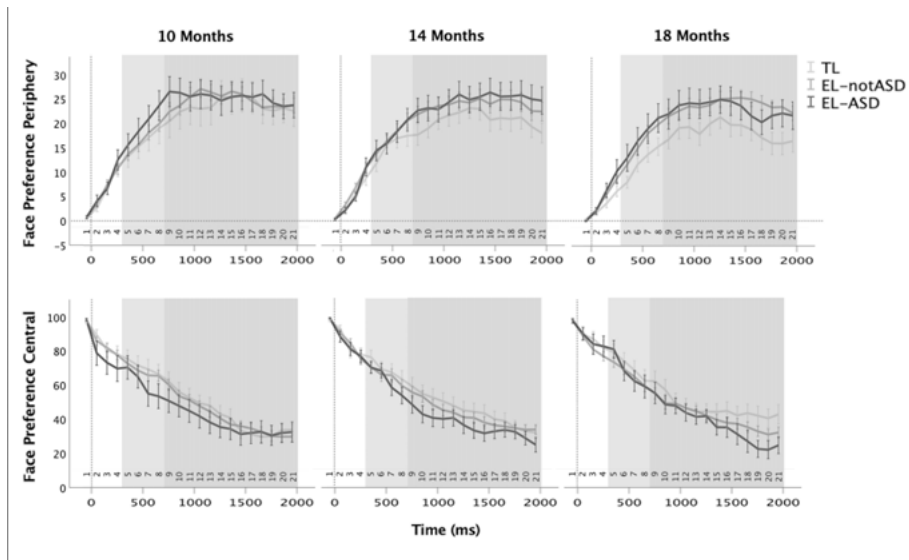
Where the infant looked before the direct-gaze event affected the subsequent gaze behaviour: If the infant was looking away from the adult's face before the direct-gaze event they could respond by shifting their gaze towards the face, but if the infant was already looking at the adult's face before the direct-gaze event, the only change in behaviour was to look away from the face. Because the  $\Delta$  Face Preference measure included both these two instances, we also calculated two measures of Face Preference based on whether the infant looked towards the test leaders face during a 100-millisecond baseline period before the direct gaze event. *Face Preference Central* included only trials with more than 80 % of the gaze within the face AOI compared to the full scene AOI during baseline, and *Face Preference Periphery* included only trials with less than 20 % gaze within the face AOI compared to the full scene AOI during baseline. Both these measures were separately averaged across two time windows, an early time window of 300-700 milliseconds after the direct gaze event and a late time window of 700-2000 milliseconds after the direct gaze event. Only the first time window was pre-registered in the analysis plan.

Latency to look towards the adult's face (*Face Looking Latency*) likewise only included trials in which the majority (> 80 %) of the baseline period of 100 milliseconds was spent looking away from the face. Face Looking Latency was defined as the first 100 millisecond time bin after the direct gaze event of which the infants gaze was spent 100 % within the Face AOI.

Associations between the direct-gaze response measures and autism outcome were estimated using linear mixed models which included group (EL-ASD, EL-notASD, and TL) and chronological age at all three time-points (~10-, 14-, 18 months) as predictors. To estimate associations between the direct-gaze response measures and dimensional autism outcome, bivariate correlations were calculated between each measure and ADOS-2 total CSS, ADOS-2 Social Affect, and ADOS-2 Restricted and Repetitive Behaviours as well as the summed algorithm scores of ADI-R.

## Results

Infants in all three groups tended to look more towards the adult's face after the direct gaze event compared to before. The groups also did not differ in terms of looking time towards the face (divided with total looking time towards the scene). However, on a group level, infants in the TL group looked more towards the face after the direct-gaze event than infants in the EL-ASD group and the EL-notASD group. Yet, the two EL groups did not differ significantly from each other in regard to this  $\Delta$  Face Preference measure. Within the elevated likelihood groups,  $\Delta$  Face Preference did not correlate with measures of dimensional autistic traits at the 36-months outcome assessment at any of the three time points (10-, 14- and 18-months visits) after correcting for multiple comparisons.



**Figure 4.** Time series of Face Preference after the direct-gaze event (0) at each visit (10-, 14-, and 18 months), for trials in which the test leader's face was in the infants' peripheral view (upper row) versus central view (lower row) at the time of the direct-gaze event. Error bars represent standard error of the mean. The light grey box shows the Early Time Window of 300-700 milliseconds after the direct-gaze event and the dark grey box represents the Late Time Window of 700-2000 milliseconds.

The three groups did not differ in amount of face looking after the adult looked towards them in cases when they looked away from the face before the direct event (Face Preference Periphery; **Figure 4**). In contrast, in cases when the infant already looked towards the adult's face at the time of the direct gaze (Face Preference Central; **Figure 4**), the infants in the TL group tended keep looking at the adult's face significantly longer than the infants in the EL-ASD group. We found this significant group effect only in the late time-window (700-2000 milliseconds). There was no significant difference between the EL-ASD and the EL-notASD groups, and this measure also did not correlate significantly with ADOS-2 or ADI-R at the outcome assessment. In regard to how quickly the infants responded to the direct gaze by looking towards the adult's face (Face Looking Latency), there were no significant group differences between the three groups. Only one correlation between direct-gaze responses and dimensional autism was statistically significant: The correlation between Face Looking Latency and ADI-R at the 18 months' time point. Age at the three time points did not have a significant effect on either the  $\Delta$  Face Preference, the Face Looking Latency measures or overall looking time towards the face.

## Conclusions

Although atypical eye contact is a prominent aspect of autism, the results of Study II suggest that direct-gaze responses in real-life interaction are not meaningful measures to distinguish the infants who go on to develop autism from the ones who do not. Instead, we found that independent of whether they received an ASD diagnosis later in life, all infants tended to look more towards the adult's face after the direct gaze event than before, and we saw no group differences in how quickly they responded to other's direct gaze nor in how much they looked at the adult's face over-all. We also found no support for a difference in how direct-gaze responses developed during late infancy between infants with and without subsequent autism. Taken together, our findings are not in line with the notion that social attention towards faces or responsiveness to eye contact are precursors of autistic development.

In instances when the infants were already looking towards the adult's face before the direct-gaze events, the infants with subsequent autism tended to look back less towards the adult than the TL group between 700 milliseconds to two seconds after the eye contact occurred. This result is exploratory, as we did not pre-register an analysis of this late time window. However, it could suggest that others' eyes and faces does not function as a glue for attention the same way in infants with and without subsequent autism, and this finding would be in line with recent findings of faster disengagement from other's faces in autistic children (Jónsdóttir, Neufeld, Falck-Ytter, & Kleberg, 2022).

# Study III

## Background and aims

In Study III, we studied early emerging pragmatic language use and its association to autism and social and linguistic antecedents. We used decontextualized language use as a measure of pragmatic ability, which is the use of language to communicate about perceptually absent referents (Rowe, 2013; Uccelli, 2009; Uccelli, Demir-Lira, Rowe, Levine, & Goldin-Meadow, 2019). Decontextualized language use requires us to conversationally provide the context that makes the listener (or viewer or reader) understand what we refer to. Young children typically start using decontextualized language by 1.5 to 2 years age, initially with relying on conversational partners' interpretation and co-construction (Berglund & Eriksson, 2000; P. J. Miller & Sperry, 1988; Uccelli, 2009; Uccelli et al., 2019). As previously mentioned, pragmatic language use is difficult to assess, especially early in development. Decontextualized language use provides a potential early measure of emerging pragmatic language use, that could be measured already in early toddlerhood.

The aims of Study III were 1) to investigate developmental precursors to decontextualized language use, specifically how infants' core language and social communication is associated to their decontextualized language use at two years age, and 2) how early decontextualized language use in two-year-olds is associated to concurrent dimensional autism and familial likelihood of later autism.

## Methods

### Procedures

In study III we analysed the Swedish Early Communicative Development Inventory (SECDI; Berglund & Eriksson, 2000; Eriksson & Berglund, 1999), which is the Swedish version of the MacArthur-Bates Communicative Development Inventory (CDI; Fenson et al., 1994). In the questionnaire, caregivers were asked to rate their child's early linguistic and social abilities. We used two versions of the questionnaire: The SECDI Words and Gestures form which is intended for children ages 8-16 months, and the SECDI Words and

Sentences form which is intended for children ages 16-28 months. The questionnaires were sent out to the caregivers of both the EASE and BATSS studies when the infants were of ages 14 and 24 months respectively. The caregivers filled in the questionnaires online via a web survey.

## Measures and analyses

At 14 months age, we used the SECDI Words and Gestures form to extract the two independent measures. For the *Total Gesture Score*, which measured social communication, 63 items were combined over five subscales, in which caregivers rate their child's frequency of communicative gestures, play, and imitation. To form the *Core Language Composite*, which measured infant core language, we combined z-scores of the two scales Comprehension of Sentences and the Comprehension Score. In the subscale Comprehension of Sentences, the caregivers were asked to mark which out of 27 early phrases that their child comprehended (such as "clap your hands"), whereas the Comprehension Score consisted of a checklist of 370 common, early words of which the caregivers marked which ones their child comprehended.

At 24 months age, we used the SECDI Words and Sentences form to extract the main dependent measure The Pragmatics Scale, and the secondary control measure The Grammar Scale. *The Pragmatics Scale* consisted of five items measuring decontextualized language use with a possible total score of ten: 1) Does your child ever talk about things that have happened before? 2) Does your child ever talk about things that are going to happen in the future? 3) Does your child ever talk about things that are missing, e.g., if a doll has disappeared or about people that are not present? 4) Does your child understand if you ask about something that is not immediately present, i.e., if you ask your child to get a toy from another room 5) Does it ever happen that your child picks up or points towards another person's object and speak the name of that person? *The Grammar Scale* consisted of six items, with a possible total score of 12, wherein the caregiver marked whether the child use common, early grammatical markers of the possessive, singular, plural, past tense, and supine forms (which are common in Swedish).

The relative contribution of the Core Language Composite and the Total Gesture Score at 14 months on the Pragmatics Scale at 24 months was estimated in the Combined Typical Likelihood Group, using a hierarchical regression analysis with the two predictors as independent

variables and the Pragmatics Scale as dependent variable. Associations to likelihood of ASD was estimated in the EASE sample by including likelihood group as a main and interaction term to the model above. We also compared the SECDI measures between the EASE typical likelihood group and elevated likelihood group using one-way ANOVAs. Associations to dimensional autism were estimated as correlations between the Pragmatics Scale and concurrent ADOS-2 scores at 24 months age. As secondary, more explorative analyses that were not pre-registered we 1) estimated the relative contribution of the Core Language Composite and the Total Gesture Score at 14 months age on the Grammar Scale at 24 months age, and 2) performed twin analyses to estimate the influence of shared genetics and environment on the Pragmatics and the Grammar Scales at 24 months age (description and results of that second analysis can be found in Paper III).

## Results

For infants in the general population, sampled here in the combined typical likelihood group of the EASE and the BATSS studies, core language and social communication at ~14 months interacted in predicting decontextualized language use at ~24 months age. A moderation analysis showed that social communication behaviour was a significant predictor only when the child had low levels of core language. There was no significant effect of likelihood group on the regression model, suggesting that the relation between infant core language and social communication and later decontextualized language use does not differ depending on family history of ASD.

Children with higher scores on the ADOS 2 tended to be rated as using less decontextualized language use with a significant negative correlation between the pragmatics scale and both the ADOS-2 total CSS score and the two subscales ADOS-2 SA and RRB. The association between ADOS-2 and decontextualized language held despite adding concurrent core language use (measured with the grammar scale of SECDI) and non-verbal developmental level (measured with the MSEL NVIQ) as covariates, while neither of these two covariates was a significant predictor. In contrast, neither the Total Gesture Score nor the Core Language Composite correlated significantly with the ADOS-2. The children with an elevated likelihood of receiving a diagnosis themselves

used decontextualized language less than their peers with typical likelihood of autism. This group difference was not explained by concurrent core language (measured with the Grammar Scale). The groups did not differ significantly on neither core receptive language or socio-communicative behaviours at 14 months age, nor on core language use at 24 months.

## Conclusions

In Study III we found that at two years' age, the pragmatic ability of decontextualized language seems more closely associated to infant core language than social communicative behaviours. For children whose core language was on a lower-than-average level at 14 months, their social communicative abilities might to some degree help compensate in the development of decontextualized language.

We also found that decontextualized language use was associated to dimensional autistic traits already at two years age. Furthermore, children with an elevated likelihood of receiving an ASD diagnosis were rated to use decontextualized language less than their typical likelihood peers. To our knowledge, this study is the first to show a possible association between autism and pragmatic language use this early in life. Given that the association between decontextualized language use and autism was not explained by concurrent developmental level or core language use, together with the finding that core language did not differ between groups at either 14 or 24 months, our results suggest that decontextualized language is independently and specifically associated to autism in a way that core language is not. As such, we reason that decontextualized language use may indeed be reflecting pragmatic ability already this early in development.

# General discussion

When going through life, we are constantly met with a multitude of information. Some of that information functions to make the transferral of communication easier. Such facilitation of communication can take the form of basic communicative cues, such as speech sounds or the direct gaze, functioning to alert others that communication is ensuing. But it can also take the form of more nuanced communicative moderators in the form of pragmatic language use, for example to make us understand the context of what is being said. How we respond to communicative cues early in development may affect what we perceive and learn from the environment. How we use communicative facilitators ourselves in early childhood may affect the effectiveness of communication and our experience of social interaction. Communicative facilitators are therefore important aspects of communicative interaction and development.

The aim of this thesis was to investigate the relation between some aspects of early communicative facilitation and autism. Study I and II focused on infants' responsivity to others' communicative cues. In these two studies we investigated if early sensory responsivity to sounds and behavioural responses to direct gaze can be regarded as developmental precursors of autism. For Study III the focus moved to later in the development of communicative facilitation. We investigated the association between early dimensional autism and the use of the pragmatic subskill of decontextualized language. In the following sections I will discuss the findings of these three studies. First, I will go into a more detailed discussion of each study in relation to the aims of the thesis. Following that is a discussion of the findings in relation to both their theoretical and practical implications. Lastly, I will discuss some important limitations and suggestions for future directions of study, and end with a brief conclusion of the thesis.

## Responses to facilitators of communication in infancy

The first aim of this thesis was to investigate infant responsivity to other's communication facilitating cues in relation to the development of autism. This was done in two studies: In Study I we investigated infant attentional responsivity to speech and non-social sounds, and in Study II we investigated infant behavioural responses to other's direct gaze. In both Study I and II we investigated associations with autism and if these two aspects of early communicative facilitation can be regarded as early precursors of autistic development.

### Pupillary responsivity to sounds in infancy

In study I we investigated infants' responsivity to social and non-social sounds through the use of pupillometry, reflecting activation of locus coeruleus and noradrenergic release. The results suggested that infant attentional responsivity to sounds might indeed be a developmental precursor of autism. The infants who later met the criteria for an ASD diagnosis had stronger pupillary reactivity to the non-social sound of running water than the infants without subsequent diagnosis. These results suggest that even before the manifestation of clear signs of autism, there are basic differences in basic sensory and attentional functioning between infants with and without subsequent autism. This finding is in line with hypotheses of differences in basic sensory systems being an important driver of autistic development (Mercati et al., 2017; Rubenstein, & Merzenich, 2003). In contrast, we found no group differences in pupillary responses to the social sound of infant-directed speech. Therefore, the differences in basic auditory responsivity that we found in Study I does not seem to be specifically linked to the communicative cue of speech, and these results suggest that responsivity to communicative facilitators in the form of social sounds is not necessarily an early marker of autistic development. Yet, atypical responsivity to sounds in infancy might still have cascading consequences on the development of communication, as is discussed under the heading of *Theoretical implications*.

The findings of Study I were unexpected. We had hypothesised that if we were to find significant group differences, these would follow one of these two potential patterns: 1) That the infants with subsequent autism would react stronger to both conditions, due to general hyper-responsivity to sounds in autism (Baranek et al., 2006; Clifford et al., 2013; Watson et al., 2011), or 2) that the infants without subsequent autism would react stronger to the social condition due to the saliency of that stimulus in typical development (e.g. Vouloumanos & Werker, 2007). Instead, we found group differences only in the non-social sound condition, and striking similarities in pupil dilation to the social sounds between the groups. I discuss potential explanations of these results below, but first I want to acknowledge that these interpretations are

constructed after we saw the results, which does not provide as strong scientific value as if we had generated these hypotheses from theory and specifically tested them in this study. Nevertheless, I will start with the finding that the infants with subsequent autism dilated their pupils more in response to the non-social sounds than the infants in the other two groups. A possible interpretation is that the non-social sounds, or more specifically the repetitive sound of running water, is particularly attention-grabbing for infants with subsequent autism. Because the two sound conditions differ in more ways than being social or non-social, it is not possible to pin-point exactly which aspects of the sounds that elicited the difference in response between the groups. For example, in the waveforms and spectrograms of the four sound stimuli in the appendix of Study I it is apparent that the acoustic characteristics differ greatly between the two types of sounds. Instead of being due to the fact that the sound of running water is non-social in nature, the group differences could be due to some acoustic characteristics of the sounds, like for example the repetitiveness of the sounds. I continue with the finding that the three groups did not differ in their pupillary responsivity to the social sounds. This could mean that responsivity to speech sounds is not a precursor of autism, and that the infants therefore do not differ in their reaction to that sound. However, we do not know if there are differences in basic sensory processing of the speech sounds between the groups that is not reflected in pupil dilation differences. For example, it is possible that speech is more salient for the typically developing infants, but that this difference is concealed by general sensory hyper-responsivity in the infants with subsequent autism. An argument against this interpretation is the difference within the EL-ASD group between the conditions, meaning that the infants with subsequent autism reacted stronger to the non-social sounds than they did to the social sounds (**Figure 2**). General hyper-responsivity in infants with subsequent autism would namely predict more pupil dilation to both types of sounds. The conclusion of this paragraph is that we cannot know precisely the processes behind the patterns of results of Study I. However, what we can conclude is that basic attentional responsivity to sounds seem to differentiate infants with subsequent autism, and that this pertains not specifically to social sounds, but rather either to non-social sounds or to sounds in general.

Pupil dilation, which was used as a measure of basic attentional reactivity, reflects not only changes in light conditions, but also changes in the brainstem kernel of locus coeruleus (Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2017; Joshi, Li, Kalwani, & Gold, 2016; Laeng, Sirois, & Gredebäck, 2012; P. R. Murphy, Robertson, Balsters, & O'connell, 2011). Locus coeruleus has a central role in the release of noradrenaline throughout the brain (Larsen & Waters, 2018; Reimer et al., 2016), which has been linked to arousal, sensory processing, memory consolidation, attentional shifting, and selecting to focus on certain stimuli over others (e.g. Aston-Jones & Cohen, 2005; Bast et al.,

2018; Berridge & Waterhouse, 2003; Geva et al., 2013; Mather et al., 2016; Sara & Bouret, 2012). Atypical attentional functioning, LC-NE activation and arousal regulation has been implicated as early emerging and potentially important factors of in autistic development (Baranek et al., 2013; Bast et al., 2021, 2018; Keehn, Müller, & Townsend, 2013). Autistic children and adults have repeatedly exhibited atypical tonic arousal, with larger-than-normal pupil size (Anderson & Colombo, 2009; Fan et al., 2009). In regard to phasic arousal, meaning arousal in response to changes in the environment, findings have been more mixed, with evidence for both typical and atypical phasic pupil dilation in autism (e.g. Bast et al., 2018; Keehn et al., 2013; Kleberg, Thorup, & Falck-Ytter, 2017). Our results suggests that atypical phasic arousal and activation of the LC-NE are indeed present in the early development of autism, and are therefore in line with the view that basic attention and responsivity to exogeneous stimuli could be fundamental to autism.

Independent of the cause of the differences in attentional responsivity to sounds in autism, such differences in attention can have cascading effects on memory, learning, cognition and behaviour (Aston-Jones & Cohen, 2005b; Mather et al., 2016; Sara, 2009). Indeed, in Study I we found that already in infancy, pupil dilation in response to the non-social sounds was associated on short time-scales with their gaze behaviour. While an association between LC-NE activity, attention, and behaviour had been hypothesised in infants before (e.g. Bast et al., 2018), to our knowledge this was the first time it was also shown in infants as reflecting individual variation. Furthermore, on a longer time-scale pupil dilation in response to the non-social sounds correlated with both the ADI-R and ADOS total score, as well as the Social Affect and Restricted and Repetitive behaviours sub scales of ADOS. According to the results of Study I, responsivity to sounds could therefore be linked to autism in a general way.

### Behavioural responses to direct gaze in infancy

In Study II we utilized a novel live eye tracking methodology to investigate associations between autism and infant responses to others direct gaze in a real-life interactive situation. We did not find support for viewing infant direct-gaze responses as developmental precursors of autism as neither how *much* nor how *quickly* the infants looked towards the adult's face after the direct-gaze event was reliably associated with later dimensional or categorical autism. Thus, the results of Study II suggest that even though neural processing of others' faces and gaze have been found to be predictive of autism (Dalton et al., 2005; Jones et al., 2016; Mason et al., 2022; Tye et al., 2022), these differences in social brain functioning does not seem to translate into real life direct-gaze responses in infancy.

We did find that in instances when the infants were already looking at the adult's face directly before the direct-gaze event, infants with subsequent autism tended to look away from the face more quickly than infants with typical likelihood of autism. Importantly, this measure did not differ significantly between the two elevated likelihood groups and was also not correlated to dimensional autism outcome. Therefore, this result is still in line with the general conclusion that direct-gaze responses are not reliably linked to autism in a meaningful way. In addition, this significant group difference was only found in the later, not pre-registered time window of 700-2000 milliseconds after the adult looked at the infant, with no group differences in face-looking directly after the direct-gaze event. This finding is therefore based on an exploratory analysis and should be interpreted with caution. However, if the group difference is independently replicated it could have interesting implications. There is a prevailing hypothesis of 'sticky attention' in autism, meaning that infants with subsequent autism generally exhibit slower visual disengagement from external stimuli than typically developing infants (Elsabbagh et al., 2013; Landry & Parker, 2013; Zwaigenbaum et al., 2005). However, because we found the opposite pattern, that infants with subsequent autism disengaged more quickly from the faces, our finding would rather suggest that other's faces and gaze might not function as an attentional glue in the same way in autistic and non-autistic development. This interpretation would be in line with recent findings of autistic children disengaging quicker from others' faces compared to their non-autistic peers (Jónsdóttir et al., 2022).

Longer latency to look towards the face after the direct-gaze event at 18 months was associated with higher scores of ADI-R at 36 months, but all other correlation between direct-gaze responses and dimensional autism, including both ADI-R and ADOS total score and subscales, at all three timepoints were small and statistically non-significant. In light of the overall lack of associations between direct-gaze responses and autism, the only significant correlation is difficult to interpret. Even though it warrants further investigations, we would interpret the overall results as suggesting that infant direct-gaze responses and dimensional autism are not reliably associated.

The finding that some aspects of direct-gaze responsivity did differentiate infants with elevated likelihood of autism from infants with low autism likelihood suggests that infant direct-gaze responses might be linked to genetic predisposition of autism, although not specifically to autism diagnosis or dimensional autistic traits. The results of an exploratory analysis in Study II also suggested that direct-gaze responsivity is not predictive of early ADHD or developmental language disorder diagnoses. Notably, at three years age those diagnoses should be regarded as provisional, as it is an early age for diagnosis. This exploratory result should therefore be interpreted with caution. Yet, these findings raise the question of why direct-gaze responsivity seem associated to

autism-likelihood, but not to diagnosis per se. It is possible that direct-gaze responses in infancy does not clearly map onto diagnostic categories or dimensional aspects of these neurodevelopmental conditions. As mentioned in the introduction, co-occurring conditions are very common in autism and there is genetic overlap between several neuropsychiatric conditions that lead to aggregation within families (Mannion & Leader, 2013; Matson & Goldin, 2013). Because atypical eye contact is not a behaviour that is unique to autism, another possible explanation is that direct-gaze responses in infancy are associated with some other commonly co-occurring condition that we have not tested here, for example social anxiety (Corden, Chilvers, & Skuse, 2008; Hessels, Holleman, Cornelissen, Hooge, & Kemner, 2018).

## Use of communicative facilitators in toddlerhood

The second aim of this thesis was to investigate young children's ability to facilitate their own communication and its' association to autism. In Study III we therefore shifted focus from early markers of autistic development onto functional communication in toddlerhood. More specifically, we studied two-year-olds use of the pragmatic ability of decontextualized language; how it is associated to dimensional autism and familial likelihood of autism, as well as to infant use of core language and social communication. We found that already early in language development, parents' assessment of their child's use of decontextualized language was negatively associated with dimensional aspects of autism assessed by clinicians, as well as with having familial elevated likelihood of developing autism. Thus, having family history of autism and exhibiting more autistic traits in toddlerhood was associated to talking less about things and events beyond the here-and-now. The association between this early pragmatic language aspect and dimensional autism was not explained by general developmental level measured with MSEL or concurrent core language level. This could imply that decontextualized language, as a measure of early pragmatic language, is independently associated to autistic traits already in toddlerhood.

To better understand the early development of decontextualized language in general, and not only in association to autism, we also investigated its associations to infant core language and social communication in our sample representing the general population (the combined typical likelihood group). This analysis showed that 2-year-olds' use of decontextualized language was more strongly associated to infant core language than social communication, implying that at least early in development, core and pragmatic aspects of language are linked. As briefly mentioned in the introduction of this thesis, there is an ongoing theoretical debate on the association between pragmatic and core language, and whether they are best regarded at two aspects of an underlying

language faculty or as distinct abilities with different underlying cognitive antecedents (Carston, 2002; A. C. Wilson & Bishop, 2019, 2021a). The finding that infant core language was linked to decontextualized language in toddlerhood is in line with the hypothesis that at least early in development these two aspects of language could be quite closely associated (Carston, 2002; A. C. Wilson & Bishop, 2019, 2021a). The results of the twin analyses of Study III (see description in Paper III) suggested different aetiological influences of genes and environment between core and pragmatic language. This might suggest that even though core and pragmatic language are strongly linked, they are still dissociable aspects of language ability already in toddlerhood.

We found that core language moderated the association between social communication and decontextualized language: Infant social communication predicted decontextualized language use at two years age only in infants with lower levels of core language ability. It is possible that this interaction reflects that social communicative abilities might to some degree compensate for lower levels of core language in pragmatic development. Whereas this pattern was found in our combined typical likelihood sample, it is not fully clear from the results of Study III if this interaction extends also to infants with elevated likelihood of autism. On the one hand, when combining the infants with and without elevated likelihood of autism, the links between infant core language and social communication and 2-year-olds' decontextualized language was not moderated by autism likelihood. On the other hand, in an exploratory analysis of these associations within the elevated likelihood group separately, there was no interaction between social communication and core language. It is possible that this separate analysis, with a smaller sample, lack the statistical power to detect such an interaction. Yet, if the lack of an interaction between core language and social communication is replicated in an independent sample, it could be that the potential protective aspect of social communicative abilities in compensating for lower core language levels is not as prominent in infants with familial history of autism.

## What does Study I-III tell us about facilitators of communication and autism?

The overarching aim of this thesis was to investigate the association between three early aspects of communicative facilitation and the development of autism. In Study I, we found that infant attentional responsivity to sounds may be an early marker of autism, but that this connection was not specific to the communication facilitating cue of speech. The results of Study II suggested that infant behavioural responses to others direct gaze is not a reliable predictor of autistic development or later ASD diagnosis. As such, these two aspects

of responding to other's communication facilitating cues in infancy does not seem particularly linked to autism. In Study III, we found that caregiver reported infant social communication and core language was not markedly different between infants with and without elevated likelihood of autism. Yet, already by age two years these two groups differed in their pragmatic language use, measured as decontextualized language, and this aspect of facilitating communication was independently linked to dimensional autistic traits measured by the ADOS. As such, despite the lack of a connection between autism and *responding* to facilitators of communication in infancy, a connection was found between autism and *using* facilitators of communication in toddlerhood.

The fact that we found no link between autism and facilitators of communication in Study I and II, but did find it in Study III could potentially be due to the differences in ages studied (infancy versus toddlerhood). If so, we would expect toddlers with and without subsequent autism to differ in terms of responsiveness to communicative cues in toddlerhood - something that we have not tested in any of our studies. If responsiveness to facilitators of communication is better regarded as an aspect of autism rather than a precursor to autistic development, this would be in line with other studies not finding clear, behavioural signs of autism until after the first year of life (Elsabbagh, 2020; Elsabbagh & Johnson, 2010; Falck-Ytter, Bölte, & Gredebäck, 2013; Jones et al., 2014). Going against this interpretation is the fact that we found no effect of age between 10 to 18 months in either Study I or II. After all, 18 months age is only half a year younger than the age in which we found differences in Study III. Therefore, our results does not clearly support the interpretation that age is the main reason we do not find differences in early responsiveness to communicative cues in autism. This is further discussed under the heading *Developmental change over the first two years of life* below.

Another possible reason for the difference in findings of Study I-II versus Study III is that the first two studies are about *responses* to communicative facilitators whereas the third study is about *initiating* or *using* facilitating aspects of communication oneself. This second explanation would be in line with what Nyström and colleagues (2019) found in regard to infant joint attention and autism. They found that *responding* to others' bids for joint attention did not differentiate infants with and without subsequent autism, but that *initiation of* joint attention did: Infants with subsequent autism used cues to initiate joint attention significantly less than the infants without subsequent autism (Nyström et al., 2019). To respond to others' communicative cues involves different processes than initiating and facilitating communication does. To notice communicative cues, which is a prerequisite to be able to respond to them, partly relies on social attention - to orient towards socially important and salient aspects of the environment. Beyond the main findings of Study I and II, we also found no group differences in preference for social, biological

motion in study I or in general orienting towards the face in Study II. Such social attention and orienting has been found to be similar in typical and autistic development also in other studies of infants (e.g. Elsabbagh et al., 2013; Falck-Ytter et al., 2018). It is therefore possible that the findings of Study I and II reflect a lack of atypical social attention and orienting in early development of autism, which in turn results in a lack of differences in responsivity to facilitators of communication. The ability to produce and facilitate communication oneself requires several social and cognitive skills. For example, to communicate effectively we need to be able to flexibly allocate our attention and integrate information from different sources, only some of which are social. Such information processing has been implied to differ between autistic and non-autistic people (Cruys et al., 2014; Fletcher-Watson & Bird, 2020; Mottron, Dawson, Soulières, Hubert, & Burack, 2006; Murray, 2018; Murray, Lesser, & Lawson, 2005; Pellicano & Burr, 2012). Both a lack of specifically social attention and an existence of general processing differences in autism could thus explain the differences in findings between Study I-II and III, and this is further discussed under the heading *Theoretical implications* below.

## Developmental change over the first two years of life

In neither Study I or II did we find a significant interaction between age and group over the period of 10- to 18 months age on any of the measures. This means that during this period in infancy, the differences between groups (EL-ASD, EL-notASD, and TL) does not seem to change with age for neither responsivity to sounds nor direct-gaze. Furthermore, in Study III we found that whereas the infants with an elevated likelihood of autism scored lower on the decontextualized language measure at two years age than the typical likelihood group, they did not exhibit significantly less receptive core language or social communicative abilities when they were around one year of age.

These findings were surprising for two reasons. Firstly, previous research have shown that group differences in measures which are predictive of autistic development are frequently moderated by age (e.g. Hazlett et al., 2017; Nyström et al., 2019). More specifically for social communication, infants with and without subsequent autism have been found to have more diverging developmental trajectories of social smiles, vocalizations and gazes to faces with age (Ozonoff et al., 2010). Thus, while behaviour in infants with and without subsequent autism tend to start out at a quite similar points, with small (if any) group differences during the first year of life, autistic and non-autistic developmental trajectories diverge more and more over the course of the second year of life (Elsabbagh, 2020; Elsabbagh & Johnson, 2010; Falck-Ytter et al., 2013; Jones et al., 2014). Yet, this is not what we find in Study I and II. However, although we did not find significant linear interactions between age

and group in our studies, that does not mean that individual developmental trajectories does not differ during this period of life. Indeed we do find quite large individual variability in regard to both responsivity to sounds and direct gaze, and this individual variability might not map clearly onto our clinical outcome groups. The lack of an interaction effect between age and group for the measures of Study I and II might therefore reflect heterogeneity of developmental trajectories in the development of autism.

Secondly, general delay in both core language and social communication has been found to be common in the broader autistic phenotype already by the end of the first year of life (Toth, Dawson, Meltzoff, Greenson, & Fein, 2007). In previous studies, also using the CDI, infants with a family history of ASD differed from typically developing infants in regard to both receptive core language and social communication at this age (Lazenby et al., 2016; Zwaigenbaum et al., 2005). Furthermore, clear behavioural signs of autism often start being manifested around age one (Elsabbagh & Johnson, 2010), and this is true also for social and communicative aspects with group differences related to social orienting, eye contact, and communicative gestures (Zwaigenbaum et al., 2013). The results of Study III is difficult to reconcile with these previous findings. Perhaps they could be an important reminder of the difficulty of finding clear and consistent patterns of development in autism.

Taken together, the results of the three studies of this thesis suggests that the developmental trajectories of responsiveness to communicative facilitators does not seem to be distinctly different in autistic versus non-autistic development. By age one infants with and without elevated likelihood of autism does not necessarily differ in how their caregivers rate their development of social communication and language. Yet, by the time they reach two years they already show differences in their development of pragmatic language use.

## Theoretical implications

In the following sections I will relate the findings of Study I-III to theoretical accounts of the development of autism. First, I will discuss the results in relation to the theoretical debate regarding if early development of autism is better understood from a domain general or specifically social account. As a short reminder, the *social first* account proposes that autism is caused by early atypicalities in social motivation and processing (e.g. Chevallier et al., 2012; Dawson et al., 2004; Klin et al., 2015). These early atypicalities are hypothesized to lead to less social learning opportunities and in turn to atypical social behaviour in autism. The competing *domain-general processing* account instead suggest that basic and early atypicalities in autism are widespread and

not specifically social (e.g. Cruys et al., 2014; Elsabbagh & Johnson, 2016; Pellicano & Burr, 2012). This account instead focuses on early attention, perception and sensory processing as crucial factors of autistic development.

Even though Study I and II are not specifically testing hypotheses related to these two theoretical accounts, the results of these studies are more in line with the domain general account than the social first model. Specifically, we did not find support for early differences in distinctly social orienting in autism. In Study I we found no differences between the infants with and without subsequent autism in their attentional responsivity to the social sounds of speech or in how much they oriented towards the visual biological motion. As previously discussed, we cannot say precisely which processes drives that pattern, but the most parsimonious explanation suggests that infant reactivity to sounds in autism is either domain general or related specifically to features of the non-social sounds. In Study II we found that responses to other's direct gaze was not a reliable predictor of autism outcome. Instead, all infants tended to look more towards the adult's face shortly after the adult looked towards them, and we also found no group difference in how the infants spontaneously oriented towards the adult's face during the social interaction. While neither preference for biological motion nor orienting towards the face were primary analyses with specific hypotheses in these studies, the results add to the general interpretation that social attention and orienting in infancy does not seem markedly different in infants with later autism. In contrast, we found sensory and attentional atypicalities in autism that were not specifically linked to social stimuli, in line with the domain general account: The group differences in pupil responses to the non-social sounds in Study I suggest that there are basic attentional differences in the early development of autism.

These findings raise the question of how early domain-general atypicalities, such as what we found in Study I, could lead to the social and communicative difficulties that we find in Study III. In the following sections I will discuss some potential explanations for this. First it is important to note that the developmental relationship between sensory, attentional and social aspects of autism likely are interacting and interdependent. For example, sensitivity to loud noises could lead to avoidance of social or communicative situations that are noisy. Likewise, an attentional system that prioritises non-social stimuli might miss others' communicative cues. Both of these scenarios could result in less social learning situations, less successful communication, and in turn avoidance of social stimuli and settings.

Social and communicative information is complex, and social interaction is fast and dynamic. Social and communicative functioning therefore puts high demands on processing abilities, integration between top-down and bottom-up information, and attentional flexibility between different sources of

information. It might be that these attributes of social communication help explain how early atypicalities in general information processing can be the basis of a condition that is largely manifested by social and communicative difficulties. Due to the complexity of social information, it can be regarded as a special, complex case of information processing, making it extra susceptible for atypical information processing and cognitive flexibility in autism. For example, autistic perception and information processing has been found to be characterized by more reliance on bottom-up sensory information than top-down interpretation, predictions and contextual information (Cruys et al., 2014; Mottron et al., 2006; Pellicano & Burr, 2012). This pattern is hypothesised to explain the strengths in visual search and pitch perception often found in autistic individuals (Happé, 1999; Meilleur et al., 2015). However, that same tendency could also lead to difficulties in social and communicative functioning, as these abilities requires flexible and dynamic integration of contextual and previous knowledge with the concurrent multi-sensory social information. Something that an autistic mind might not be as inclined to do.

Another, not mutually exclusive, explanation of the link between early general processing abilities and later communicative ability is more specifically linked to attentional functioning. According to the *monotropism* account, peoples' attentional functioning can be placed on a spectrum from *monotropism* on one end, meaning high focus on one source of information at a time, to *polytropism* on the other end, meaning a tendency to attend to multiple sources of information simultaneously. In this account autism is defined by a highly *monotropic* attentional system (Murray, 2018; Murray et al., 2005). A highly *monotropic* attentional system would have strengths for example with identifying details, but have difficulties with flexibly integrating top-down and bottom-up information, like in the explanation above. Beyond that, a highly *monotropic* system might also miss social and communicative cues due to directing the attention towards another source of information due to the tendency to prefer information from one source at a time (Fletcher-Watson & Bird, 2020). For example, in Study I the social and non-social sounds were played in succession, and never simultaneously. It might be that if we presented the two sounds simultaneously, then infants with and without subsequent autism might have differed more in regard to the social sounds due to different attentional capture by the non-social sounds.

The *monotropism* account was originally proposed by autistic scholars and is a popular explanation of autistic functioning for many autistic people (Milton, 2012; Murray et al., 2005; Williams, 2021). A related model, that also originates from autistic scholars, is the *sense-making* account (De Jaegher, 2013). Information transfer has been found to be more effective between two people of the same neurotype, meaning between autistic to autistic persons and non-autistic to non-autistic persons, than between an autistic and non-autistic

person (double empathy; Milton, 2012). This finding has led to an increasing conception of communicative dysfunction as a property of the communicative situation rather than an intrinsic property of the communicative partners (De Jaegher, 2013; De Jaegher & Di Paolo, 2008; Williams, 2021). This is the core of the sense-making account, and such a dynamical systems perspective of communication and pragmatics resonates with the neurodiversity perspective. When combining the sense-making and monotropism accounts, communicative difficulties in autism are interpreted as originating in the difficulty of communication between two functionally different cognitive systems (Williams, 2021). From that perspective, the early differences in attentional responsivity that we found in Study I could reflect a basic difference in attention allocation. Such early differences might, through developmental cascades exemplified above, lead to large differences in perception, cognition and functioning. So large differences, in fact, that two people with different early and basic attentional systems would have difficulty in transferring social information between them – in communicating. The basic differences in attention allocation and sensory responsivity found in study I, could thus be reflecting the initial stages of diverging developmental trajectories that, through interaction with other cognitive, behavioural and environmental modifiers, throughout the first and second year of life, lead to the associations between autism and functional communication that we found in Study III.

## Practical implications

The three studies of this thesis were aimed towards a better understanding of the developmental processes of autism in the first years of life. While studies of early developmental antecedents of autism and functional communication have the prospect of earlier identification of infants at risk of having later problems as well as earlier intervention to alleviate that risk, neither of the studies were specifically targeted towards these goals. Nevertheless, the results of the three studies still have some practical value, beyond their original aims. Study I employed a pupillometry paradigm, which is still novel within the field of infant autism research. Pupillometry is relatively easy to perform and analyse. It is non-intrusive, which makes it particularly suitable for infants. The findings of Study I suggested that pupil dilation to the non-social sounds was linked to autism in terms of both categorical diagnosis and dimensional autistic traits associated to both social functioning and restricted behaviours. If these findings are replicated in independent samples, and early pupil responsivity to sounds proves to be a robust predictor also on an individual level, then early pupillometry to sounds might show potential as an early screening method of infants in the setting of regular health check-ups. In Study II we studied infant behaviour in a real-life interactive situation, using novel live eye tracking methodology. We found that on a behavioural level, direct

gaze responsivity was not reliably associated to autism. Previous studies on early responsivity to eye gaze and face have found that the type of stimuli and context of experimental tasks affect whether autistic participants perform similarly to neurotypical participants (Guillon, Hadjikhani, Baduel, & Rogé, 2014; Hessels et al., 2018; Speer, Cook, McMahon, & Clark, 2007). General ‘truths’, such as atypical eye contact being a hallmark expression of autism and one of the earliest signs of the condition, might not always be supported by more exact measurements, especially not when measured in real-life situations. The results of Study II can therefore be a reminder of the importance to test behaviour in ecologically valid settings and to generally be careful in how we interpret behaviours that arise from complex contexts.

## Limitations

The conclusions of Study I-III should be interpreted in light of a number of limitations. First, it is important to consider both the validity of our conclusions and the reliability of our findings. The three studies of this thesis spans from high to low control and therefore also between high to low generalizability. In study I we performed an experiment in which we have high control of the measurements and variables, but also potentially less generalizability the real-world settings and situations. For example, we only tested one type of non-social and one type of social sounds. We therefore cannot know whether our results generalize also to other types of sounds. Furthermore, the embedding of the experiment within a paradigm of biological motion leads to concerns in regard to ecological validity and generalizability also to other situations. In Study II we moved to a more ecologically live eye tracking setting. This meant that we can draw conclusions that pertain to real-life infant behaviour. However, this also meant that we gave up some control over what we are measuring. As previously stated, social interaction is complex and therefore we are probably not capturing all processes that are going on in that situation. In Study III we had the least control over our measurement as they were based on parental report questionnaires. This is a limitation due to common method bias and because it can be difficult for a parent to rate their own child in general. We cannot know if all caregivers interpreted the task of the questionnaires the same way, or if they differ in their ratings of their children’s communicative development. However, because pragmatic language is notoriously difficult to capture in formal testing situations, especially for young children, we concluded that parental ratings still constitute a good estimation of young children’s real-life behaviour. Still these aspects of the three studies limit either the generalizability or the reliability of the conclusions.

In both the EASE and BATSS studies, infants were recruited from the greater Stockholm region, including the university town of Uppsala. In accordance, the participating children generally had parents with high educational level and socio-economic status and most were native Swedish. The generalizability of the results of this thesis to other backgrounds and cultures might therefore be limited. In relation to Study II for example, eye contact, interpretation of direct gaze, and responses to gaze-shifts differs largely between cultures (Akechi et al., 2013; Senju et al., 2013). While basic orienting and attentional responsivity to direct gaze have been found to not differ between cultures in adults (Akechi et al., 2013; Senju et al., 2013), it is important to be careful when interpreting especially social behaviours as universal. Similarly, in Study III we measured social communication and language use – aspects that are different between cultures and associated to socio-economic status (Fenson et al., 1994; Matthews et al., 2018). Notably, socio-economic status has previously been found to not have a significant effect on language development in Swedish settings (Berglund, Eriksson, & Westerlund, 2005), and we found no correlation between caregivers' educational level and any of the measures on social, communicative and linguistic skills. Yet, the development of decontextualized language use, and the importance of that pragmatic function, might still differ between languages and cultures. Beyond this, we also do not know if the results of Study I-III generalizes to children with lower developmental levels and IQ (Brown, Chouinard, & Crewther, 2017).

In infant sibling studies we study only inherited autism in infants that are part of multiplex autistic families. Therefore we cannot know if the results of our studies generalizes also to autistic children with other forms of autism, for example as part of a genetic syndrome (Virkud, Todd, Abbacchi, Zhang, & Constantino, 2009). Furthermore, because the infants in the elevated likelihood groups all have autistic family members, their home environments are likely to differ in some regards from the typical likelihood infants. Autistic parents and siblings might interact with their infants slightly differently than non-autistic families would (e.g Freeman & Kasari, 2013). Based on the double-empathy account, an autistic parent might even interact differently with their own child depending on whether they have autism or not, potentially even leading to environmental differences between the two elevated likelihood groups. Most importantly for the conclusions of this thesis, we do not know about these processes and how they potentially affect development in our particular studies. Therefore, one should be careful to not interpret differences in early autistic development as being purely due to genetic differences between groups. A related issue concerns specifically Study III. It is possible that caregivers of children with autism rate their other infants differently than caregivers of typically developing children. For example, they might rate the younger sibling as less or more atypical in comparison to the older sibling(s). However, while this limitation could affect between-individual results (such

as group differences), it should not affect the within-individual measures (such as the correlations with dimensional autism or developmental precursors) that are the main findings of Study III.

In Study I and II, where the participants were divided into three groups based on likelihood and diagnosis of autism, the sample sizes are limited, particularly in the EL-ASD group. While our sample sizes are comparable to most other infant sibling studies (e.g. Elsabbagh et al., 2012; W. Jones & Klin, 2013; Macari et al., 2021; Ozonoff et al., 2010), statistical power is still a concern. In both Study I and II we do find significant group effects that include the EL-ASD group, which would indicate that the statistical power is sufficient, but replications in independent, preferable larger samples are necessary.

## Future directions

As most research tend to do, the studies of this thesis have resulted in more new questions asked than old questions answered. Therefore, I have ideas for possible future direction of each study. For Study I, I would like to delve deeper into which aspects of the non-social sound seem to draw the attention of infants with subsequent ASD. *Why* is it that the sound of running water draws the attention of some infants more than others? Because Study I is the most controlled and least naturalistic of the three studies of this thesis, I would also like to know if the results of Study I are valid outside of the lab, in real-life situations. A future direction is to test if autistic children differ in regard to which sounds they attend to also in typical, real-life situations, like in the breakfast scene described in the beginning of this thesis. For Study II, an unanswered question is why direct-gaze responses seem to be associated to having elevated likelihood of autism but not to receiving an ASD diagnosis. A future direction would therefore be to further investigate the effect of less infant direct-gaze responses on development, and whether this phenotype is linked to other commonly co-occurring conditions with overlapping genetic aetiology. As for Study III, there are to my knowledge no studies of the association between decontextualized language use and other pragmatic abilities. Pragmatics is a wide concept which is difficult to delineate and contains many diverse subskills (Matthews et al., 2018). I would like to follow up Study III by further investigating early decontextualized language use; If it is associated to other pragmatic skills such as narrative ability or referential communication, and if there are consequences of having an atypical or late development of decontextualized language beyond its association to autism.

The three studies of this thesis each focused on isolated communicative aspects: basic responsivity to sounds and direct gaze, and emerging pragmatic language use in toddlerhood. The multitude of methodologies and

developmental areas can be regarded as a strength of the thesis. Yet, in order to understand how autism develops, we need to step away from studying psychological aspects in isolation. While identifying markers of the earliest autistic development is still a worthy prospect, an important future goal is to also map how these early markers interact throughout development, both with each other and with other modifying aspects. Such modifying aspects could be both internal and external, and could either increase or decrease likelihood of autism. The employment of more data-driven approaches might be useful in parsing individual differences, categorizing potential subgroups to better understand heterogeneity and identifying mechanisms of different developmental trajectories. A related future direction of autism studies is an increased focus on the infants with elevated familial likelihood of autism who do not meet criteria for a diagnosis. Better understanding of why some infants do not develop autism despite predisposition for it could further our understanding of developmental processes involved in autism. Beyond that, the negative outcomes sometimes associated with the broader autistic phenotype means that this group warrants more focus and better understanding of their development.

Beyond better understanding of the complex and dynamical development of autism, another important direction is to better understand autistic outcomes. In the studies of this thesis, we have spanned an age of 10 months to three years. This is an important age span, bridging the pre-symptomatic infancy to emerging autism during the second year and into a stage when autism can be diagnosed. However, if these studies were extended into early childhood or even beyond, we could study the association between early basic communication and its later, more complex counterpart, as well as later aspects of autism outcome. Autistic outcome should not be considered only in terms of symptom severity, but also on quality of life. Furthermore, what constitutes quality of life in autism should be defined by autistic people themselves. An important step towards that direction is to include autistic people, parents of autistic children and autistic scholars more in the research process, including the decision of which areas of research should be prioritized.

Last but not least, an important future direction is to study developmental overlap and differences between the development of neurodevelopmental conditions, such as ADHD, developmental language disorder, and general learning disability. We have much yet to learn about differences in genetics, developmental trajectories, and outcome between these conditions as well as the effect of having more than one co-occurring condition. The large overlap between different conditions also warrants a continued discussion of diagnostic categories and how we are to understand atypical development.

## Concluding remarks

In this thesis I have investigated how infants respond to others' cues to facilitate communication and how toddlers start to learn to facilitate their own communication, and whether these aspects are associated to autism. The results suggests that responsivity to other's communicative cues is not a clear precursor of autistic development. Yet, already at age two years the ability to use language functionally and convey communicative context is associated to autism.

At the breakfast table in the example in the beginning of this thesis the infant had the important task of selecting which information to attend to. Based on the results of this thesis, we might speculate that if the infant is on the developmental path to autism, her brain might have a tendency to attend to the sound of running water from the tap rather than the sound of her mother's voice. However, she would be as likely as if she had a typical development to notice that her mother is looking at her and respond by looking back towards her face. If the brother who sits next to her has autism, he is likely to have difficulties in conveying the context necessary to understand that he really wants to talk about the clown at the circus yesterday. Being able to facilitate one's communication is an important aspect of our everyday lives, and one that have a tendency to complicate communication if not done accurately. Yet, based on the findings of this thesis, it might not be specifically linked to the earliest development of autism.

## Summary in Swedish

När vi kommunicerar med andra använder vi flera olika förmågor för att främja och underlätta kommunikationen. Sådana kommunikationsfrämjande funktioner kan handla om att vara uppmärksam mot andra kommunikativa signaler men även att själv kommunicera på ett sätt som gör att andra förstår. Atypisk uppmärksamhet och responsivitet gentemot sådana kommunikativa signaler har förslagits vara grundläggande aspekter av autistisk utveckling. Atypisk pragmatisk språkanvändning, det vill säga att använda språk på ett funktionellt sätt i social interaktion, betraktas istället som en viktig aspekt av autism senare i utvecklingen.

I den här avhandlingen har jag använt olika typer av metoder för att studera kopplingen mellan dessa kommunikationsfrämjande funktioner och tidig utveckling av autism. För att göra detta har jag studerat barn som har familjemedlemmar med autism, och därför större sannolikhet att själva utveckla autism än den generella befolkningen. Dessa barn följdes från att de var spädbarn upp i förskoleåldern. I Studie I testade vi spädbarns uppmärksamhet mot sociala och icke-sociala ljud med hjälp av pupillmätning. Spädbarnen med och utan senare autism skiljde sig åt gällande hur de uppmärksammade the icke-sociala ljudet, men inte gällande det sociala ljudet. I Studie II mätte vi hur spädbarn svarar på att en vuxen tittar direkt mot dem genom att titta tillbaka mot den vuxnas ansikte. I den studien fann vi att sådana blick-responser inte särskilde spädbarnen med och utan senare autism från varandra. I Studie III undersökte vi kopplingar mellan tidig pragmatisk förmåga och autism genom att be föräldrarna skatta deras små barns kommunikative förmåga. Redan vid två års ålder var pragmatisk språkanvändning associerat med dimensionell autism, oberoende av generell kognitiv och språklig förmåga

Sammantaget kan man tolka resultaten från de här tre studierna som att hur spädbarn reagerar på andras kommunikativa signaler inte är en avgörande aspekt av tidig utveckling av autism. Trots det tycks små barns förmåga att själva främja sin egen kommunikation, här mätt som tidig pragmatisk förmåga, vara associerat med autism redan vid två års ålder. Denna avhandling bidrar till vår förståelse av tidig utveckling av autism, och särskilt hur den relaterar till kommunikationsfrämjande aspekter under de första åren i livet.

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Terry Pratchett,  
*Snuff: a novel of Discworld*. Harper, New York.

But still, writing can be hard. If truth be told, the past five years as a PhD student have had their fair share of misgivings (not the least due to a pandemic). But more importantly, they have contained the joy of interesting discussions, the excitement of understanding something new, and the gratification of achieving something I did not think I could. The positive experiences are all thanks to the remarkable people that have accompanied me on this PhD journey.

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