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# Infant attentional markers studied with eye-tracking as possible predictors of toddler age adaptive behavior

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Användning av markörer för uppmärksamhet mätta med ögonrörelsemätning i spädbarnsåldern för att förutspå adaptivt beteende vid två års ålder

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Tiivistelmä – Referat – Abstract
Målsättning: Identifiering av utvecklingsmässiga utmaningar redan i spädbarnsåldern är viktigt för att ha möjlighet att inleda tidiga interventioner och därmed potentiellt öka interventionernas effektivitet. Målsättningen för den här studien var att utreda användbarheten av ögonrörelsemätning (eye-tracking) i sju månaders ålder för att förutspå adaptivt beteende i två års ålder. Adaptivt beteende beskriver barnets anpassning till hans eller hennes specifika livsmiljö och innehåller begreppsmässig, social och praktisk anpassning. I den här studien har jag använt flera markörer för visuell uppmärksamhet mätta i spädbarns åldern m.hj.a ögonrörelsemätning; sackadiska ögonrörelsers reaktionshastighet (SRT) samt preferens att rikta uppmärksamhet mot ansikten och emotionella ansiktsuttryck. Jag har undersökt de olika markörernas association till adaptivt beteende vid två års ålder. SRT är ett allmänt mått för visuell uppmärksamhet i spädbarnsåldern och har förknippats med flera utvecklingsmässiga och kliniska aspekter medan uppmärksamhetsmässig preferens för ansikten och emotionella ansiktsuttryck är markant vid sju månaders ålder och har föreslagits ha en roll i socio-emotionell utveckling. Möjlig association mellan spädbarnens tendenser för uppmärksamhetsbeteende, identifierat m. hj. a. flera olika SRT-mått, och adaptivt beteende undersöktes också.

Metoder: Den här studien använde sig av material från Toibilas-studien vid BABA-center, Helsingfors Universitets Sjukhus. Studien innefattade 45 barn, både barn utan identifierade utvecklingsmässiga risker (n=26) och barn tillhörande en hög-risk grupp (n=19) p.g.a. deras tidigare vårdperiod vid neonatal intensivvård avdelningen. Vid sju månaders ålder deltog spädbarnen i en ögonrörelsemätning med två olika uppgifter; en SRT-uppgift och en uppgift som mätte skillnaden i uppmärksamhet gentemot ansikten jämfört med annat visuellt stimulus samt emotionella ansiktsuttryck jämfört med neutrala ansiktsuttryck. Samma barns adaptiva beteende utvärderades vid två års ålder med ett frågeformulär ifyllt av en förälder. Associationen mellan markörer för visuell uppmärksamhet, barnens tendenser för uppmärksamhetsbeteende i spädbarnsåldern och adaptivt beteende i två års ålder undersöktes med lineära modeller.

Resultat och slutsatser: Större preferens för ansikten jämfört med annat visuellt stimulus vid sju månaders ålder var förknippat med bättre adaptivt beteende vid två års ålder. Upptäckten stöder hypotesen att preferensen för uppmärksamhet riktad mot ansikten är viktig för den socio-emotionella utvecklingen. En signifikant association mellan spädbarnets tendenser för uppmärksamhetsbeteende och begreppsmässigt adaptivt beteende kunde konstateras. Detta fynd tyder på att identifikation av spädbarnets tendenser för uppmärksamhetsbeteende kunde vara nyttigt för att förutspå senare utveckling. Denna studie ger preliminära bevis för principen att ögonrörelsemätning i spädbarnsåldern kunde ge kliniskt relevant infromation som förutspår utveckling, men upprepning av resultaten och framtida forskning för klinisk verifiering är av yttersta vikt.



Avainsanat – Nyckelord – Keywords
ögonrörelsemätning, spädbarn, markörer för visuell uppmärksamhet, sackadiska ögonrörelsers reaktionshastighet (SRT), preferens för ansikten, adaptivt beteende


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Tiivistelmä – Referat – Abstract


Objectives: Early recognition of developmental challenges in infancy is central for being able to start interventions earlier with possible better outcomes. The aim of this study was to investigate the potential of using eye-tracking at seven months to predict adaptive behavior outcomes at two years. Adaptive behavior implies the child's adaptation to their specific living environment and it includes aspects of conceptual, social and practical adaptation. Here, I studied several eye-tracking based markers of visual attention in infancy for their possible association with adaptive behavior at two years, such as saccadic reaction time (SRT) and measures of attentional preference for faces and emotional facial expressions. SRT has been shown to be a general attentional marker in infancy associated with many developmental and clinical aspects while attentional preference for faces and emotional facial expressions are pronounced at seven months and have been hypothesized to play a role in socio-emotional development. Infants were also studied with respect to attentional behavioral tendencies based on their SRT measures.

Methods: This study employed material from the Toibilas-study at BABA center at Helsinki University Hospital. The study consisted of 45 children of either typical development (n=26) or children of high developmental risk (n=19) due to their prior treatment at the neonatal intensive care unit. The high-risk group was assumed to increase variability of the sample. Infants participated in eye-tracking measurements at seven months old using two different eye-tracking paradigms; a SRT task and a task measuring attentional bias for facial vs. non-facial as well as emotional facial expressions vs. neutral facial expressions. The same children were assessed for adaptive behavior at two years of age by a parent filled-questionnaire. Associations between attentional behavioral markers at seven months and adaptive behavior at two years were analyzed using linear models. The models also accounted for behavioral attentional tendency as identified from a set of SRT measures.

Results and conclusions: A bigger attentional preference for faces compared to non-faces was associated with better overall adaptive behavior score as well as adaptive behavior composites for conceptual and practical adaptive behavior. This is in line with the hypothesis that attentional bias for faces is important for socio-emotional development. A significant association between identified behavioral attentional tendencies and the conceptual composite score of adaptive behavior was found. This finding suggests that recognizing attentional tendency may be useful for predicting later developmental trajectories. The present work provides preliminary evidence for the proof of principle that eye-tracking based metrics may provide clinically relevant predictions in infants, however novel prospective datasets are needed for clinical validation.



Avainsanat – Nyckelord – Keywords
eye-tracking, infant, attentional markers, saccadic reaction time, face preference, adaptive behavior


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# PREFACE

This study is part of the Toibilas-project at BABA-center, Helsinki University Hospital HUH, led by professor Sampsa Vanhatalo. The aim of the Toibilas-project is to develop new ways of using information extracted from electroencephalogram (EEG)-recordings of visually evoked potentials and -tracking measurements. This data is used to study infant attention and cognition as well as to predict later development with the specific aim of finding bio-markers with clinical potential for developing tools that could be used in developmental screening and diagnostics.

The participants of the Toibilas-study were recruited during 2015-16 in Helsinki metropolitan area. The study included different measurements at several time-points including visual evoked potentials at three months, eye-tracking at seven months and Bayley scales neuropsychological assessment at two years, including a parent-filled questionnaire measuring adaptive behavior, the adaptive behavior questionnaire (ABQ). I have been involved in collecting eye-tracking measurements.

I would like to thank professor Sampsa Vanhatalo and Susanna Stjerna at the BABA-center for allowing me with the opportunity to do my Masters thesis project in their supervision and giving me access to data from the Toibilas-project. I am also happy to have been able to learn from professor Jukka Leppänen at Tampere University and for his expertise on eye-tracking. I am grateful to all the families that participated in the Toibilas-study.

## TABLE OF CONTENTS

# 1. INTRODUCTION

Studying infant development is important for the understanding how innate abilities and environmental factors interact to produce different developmental outcomes. Earlier recognition of markers that predict maladaptive development allow for intensive follow-up of development and enables early intervention. An important aspect when searching for clinically relevant biomarkers of developmental challenges is the ecological validity of outcome measures.

The construct of adaptive behavior encompasses the daily living skills of the individual specifically with regards to the individual's adaptation to their current living environment. Adaptive behavior includes the child's ability to integrate their cognitive, social, emotional and practical skills in every day situations and is closely related to self-regulation and executive functions. Adaptive behavior disabilities are associated with later maladaptive outcomes during childhood (Barkley et al., 2002). In this study the focus is on adaptive behavior as a clinically significant construct with high ecological validity, measured by parental questionnaires at two years of age.

Studying early development in infants and their developmental trajectories has many specific challenges  (Gilmore, Knickmeyer, & Gao, 2018). Compared to older children and adults infants have limited motor ability and lack verbal communication limiting their response repertoire. Attention plays a primary role in learning and the acquisition of information. For infants regulating where they look and gaze is a central component in regulating attention and learning through the environment  (Leppanen & Nelson, 2009). Studying the development of early attention is important for advancing the field of cognitive development and can give important information on factors that influence later development as well as possible intervention targets. Eye-tracking is a noninvasive powerful tool with good spatial and temporal resolution that allows analysis of visual attentional markers in infants by following their gaze behavior (Leppanen, 2016). Eye-tracking has a potential for identifying markers in infancy that predict later outcome (Fredriksson Kaul Y 2016, Young, Merin, Rogers, & Ozonoff, 2009,  Jones, W. & Klin, 2013).

Eye-tracking studies in infancy have revealed several characteristics of gaze regulation with specific developmental trajectories. Speed and regulation of saccades, rapid eye movements that shift the point of regard, is one phenomenon that shows changes during development and is suggested to reflect basic regulation of attention (Alahyane et al., 2016; Kenward et al., 2017). Another phenomenon, hypothesized to play a role in socio-emotional development, is the visual preference for faces over other objects  (Bedford, Pickles, Sharp, Wright, & Hill, 2015; Peltola, Yrttiaho, & Leppanen, 2018)  as well as a bias towards emotional facial expressions compared to neutral facial expressions (Grossmann, Missana, & Krol, 2018; Peltola, van IJzendoorn, & Yrttiaho, 2020). Longitudinal studies are needed to understand the relevance of these developmental markers for later development. In this thesis, the aim is to study associations of specific features of these attentional markers, derived from eye-tracking measurements in infancy, with adaptive behavior at two years of age. Furthermore this study also investigates the rationale of identifying different behavioral attentional tendencies based on eye-tracking measures and if these identified tendencies should be taken into account when analyzing correlations between attentional markers and adaptive behavior outcomes.

### 1.1 Adaptive behavior

Adaptive behavior means the individual's ability to live a satisfactory life in his or her own unique living environment. The term includes the interaction between the individual's abilities and their adaptation to the environment. Adaptive behavior has been defined as "the effectiveness and degrees to which the individual meets the standards of personal independence and social responsibilities" (Grossman, 1973). Several studies have come to the conclusion that adaptive behavior in children consists of four factors (reviewed in Tasse et al., 2012) including motor or physical competence, conceptual skills, social skills and practical skills. Motor skills include both gross and fine motor skills, ambulating, and basic eating and toileting skills. Conceptual skills involve receptive and expressive language, self-direction and problem solving. Social skills include interactions with others, social participation, social problem solving, following rules, manners and friendships. Practical skills involve activities of daily living, safety, healthcare and routines (Tasse et al., 2012). The most common measuring instruments used today yield an overall adaptive behavior score as well as domain scores for the identified domains depending on the age of interest (Sparrow, Cicchetti & Saulnier, 2016, Harrison & Oakland, 2003).

To date there are no widely used laboratory tests for adaptive behavior. Adaptive behavior is measured by questionnaires or structured interviews and several measuring instruments have been developed during the years (Floyd et al., 2015). Most used measuring instruments to date, when studying adaptive behavior in children, include the Vineland Adaptive Behavior Scales (VABS, Sparrow, Cicchetti & Saulnier, 2016) and Adaptive Behavior Assessment System (ABAS, Harrison & Oakland, 2003, (Price, Morris, & Costello, 2018). ABAS-II (the second edition of ABAS) reports good psychometric properties (Harrison & Oakland, 2003).

Adaptive behavior has been discussed and criticized a lot during the years in the scientific community for still not being clearly defined (reviewed in Price et al., 2018). It was first defined in regards to the definition of intellectual disability (Tasse et al., 2012) and has in children mainly been studied in intellectual disability (ID) and autism spectrum disorder (ASD), since it is used as a diagnostic criteria in both conditions (American Psychiatric Association, 2013). Adaptive behavior in children and youths with high functioning autism spectrum disorder with normal range IQ-scores is significantly lower than what would be expected based on IQ alone from toddlerhood onward (e.g. Kanne et al., 2011; Lopata et al., 2013; Perry, A., Flanagan, Dunn Geier, & Freeman, 2009; Pugliese et al., 2015; Ray-Subramanian, Huai, & Ellis Weismer, 2011).

The validity of the construct outside these populations has remained somewhat unclear. The clinical relevance of adaptive behavior is however underlined by the fact that impairments are seen also in several other pediatric clinical groups independent of ID or ASD. Impairments in adaptive behavior have been observed in children with attention deficit hyperactivity disorder (ADHD, e.g. Balboni, Incognito, Belacchi, Bonichini, & Cubelli, 2017), brain tumors (e.g. Hoskinson et al., 2018), epilepsy (e.g. Reilly et al., 2019) and children born preterm (e.g. Taylor & Clark, 2016). A significant part of children referred to neuropsychological assessment have impairments of adaptive behavior (Papazoglou, Jacobson, & Zabel, 2013). Children with behavior problems, externalizing and internalizing problems or executive challenges have adaptive behavior problems compared with the general population (McKelvey, Edge, Mesman, Whiteside-Mansell, & Bradley, 2018; Papazoglou et al., 2013). Furthermore children with a history of maltreatment and a diagnosis of reactive attachment disorder show big impairments in adaptive behavior (Becker-Weidman, 2009). Adaptive behavior impairments are thus seen in early childhood in a wide variety of clinical conditions regardless if the etiology is primarily neurodevelopmental or environmental.

There is also some emerging evidence on the importance of the construct of adaptive behavior in children of the general population. A recent study done in an Irish sample of 2-5 year old children found that adaptive behavior had a unique contribution to children's intensity and diversity of participation in typically developing children (Killeen et al., 2018). The utility and relevance of the construct in children in the general population needs more research.

The generalizability of adaptive behavior has further been questioned because studies on adaptive behavior almost exclusively have been done in Western, educated, industrialized, rich and democratic cultures, mainly in the US (Jones, D., 2010). Adaptive behavior is dependent on the standards of the society were the individual is living and should be seen as adjustment and development, not as an attribute of the person, but as illustrative of person-environment interactions (Taverna, Bornstein, Putnick, & Axia, 2011).

### *1.1.1. Factors contributing to adaptive behavior*

The construct of adaptive behavior has high ecological validity in children, which refers to how an assessment provides clinical utility beyond diagnostic utility (Wallisch, Little, Dean, & Dunn, 2018). Adaptive behavior is closely related to the concept self-regulation (Buckner, Mezzacappa, & Beardslee, 2009). Self-regulation involves the behaviors and processes that the individual uses to modulate the overall reactivity or reactions to stimuli (Santens, Claes, Dierckx, & Dom, 2020) . During infancy, the caregiver provides much of the child's regulation. External controls on arousal, distress and sensory input eventually become internalized as toddlers come to control their own emotional and cognitive levels through self-regulation (Posner, Rothbart, Sheese, & Voelker, 2014). Self-regulation is progressing during development from simple reactive control to a more flexible, intentional, and self-directed use of attentional processes. This process allows the child to accommodate controls appropriate for a given culture and environment more and more independently (Posner et al., 2014; Santens et al., 2020). The development of self-regulation is dependent on concepts like executive functions and effortful control. These concepts are overlapping and closely related but arise from different intellectual traditions in clinical, developmental and cognitive sciences as argued by Nigg (2017) and Santens (2020). Support for the importance of these constructs for self-regulation and adaptive behavior comes from various lines of research.

Effortful control can be defined as a temperamentally based ability to inhibit a dominant response and activate a subdominant response. Temperament, in turn, can be defined as innate based individual differences in reactivity and self-regulation (Rothbart & Ahadi, 1994). Effortful control has been shown to correlate with mother-reported behavioral problems non-linearly with both high and low degrees of effortful control leading to more reported behavioral problems compared to average levels of effortful control (Murray & Kochanska, 2002).

Executive function refers to the set of cognitive processes involved in the self-regulation of emotion and goal-directed behavior (Taylor & Clark, 2016). Specific executive function domains such as metacognitive skills have been shown to affect adaptive behavior for both typically developing children and children with ASD (Gardiner & Iarocci, 2018). Children born preterm often show impairments in executive functions. The degree of impairment is bigger with extreme prematurity, neonatal complications and related brain abnormalities (Taylor & Clark, 2016).

Taken together both temperamental factors, such as effortful control, and neurocognitive factors, such as executive functioning, contribute to adaptive behavior and self-regulation. These factors are crucial for the achievement of self-sufficient living. Children who enter kindergarten without adequate self-regulatory skills are at significantly greater risk for later school difficulties. Self-regulation is correlated with different measures of life success also in adulthood, including health, income and successful human relationships (Moffitt et al., 2011).

Self-regulation can be seen as the "efficiency of executive attention" (Santens et al., 2020). Three components of self-regulation can be recognized: (1) attentional control; voluntary focus or shifting of attention, (2) inhibitory control and (3) activation control (Santens et al., 2020). During infancy attentional control is an important mean to self-regulation. During the first year of life attentional control is primarily achieved by orienting to different stimuli in the environment, controlling where to look and what to ignore (Posner et al., 2014). Orientation of visual attention can be studied in infancy using eye-tracking.

### 1.2 Eye-tracking as a means to study early markers of attention

Eye-tracking offers a method to study attention in infants and does not require any gross motor or verbal skills. Eye-tracking is an affordable, noninvasive and reliable tool that can be used with young children and infants (Boardman & Fletcher-Watson, 2017; Pel, Manders, & van der Steen, 2010) . During eye-tracking measurements a remote automatic eye-tracker uses a light source, such as a near-infrared light panel, which enables the tracker to detect gaze by creating reflections off the cornea of the eye (Venker & Kover, 2015) . An internal camera records this information and processing algorithms are applied to determine the positions of the eyes (Venker & Kover, 2015).

Eye-tracking can give insights into a wide range of questions related to specific (oculo-)motor (Goffart, Bourrelly, & Quinet, 2017) , attentional (Elison et al., 2013; Forssman et al., 2017), perceptual (Goettker, Braun, Schutz, & Gegenfurtner, 2018) , cognitive (Senju, Southgate, White, & Frith, 2009) and emotional (Fang, Sanchez-Lopez, & Koster, 2019) processes. In addition eye-tracking can be used to investigate spontaneous visual preferences and interests in complex situations that resemble real life (Keemink, Keshavarzi-Pour, & Kelly, 2019) .

Specific eye-tracking measurements could be used as screening methods already in infancy because it offers a tool that can be used in pre-verbal children still lacking sophisticated motor responses such as pointing or pressing a button. The technique also offers a possibility to be used in populations of at risk group of infants to identify individuals that have problems in visual attention or as a tool for differential diagnostics. This is illustrated by the example that enhanced visual preference for geometric repetition shows promise for being an early developmental biomarker in toddlers of an ASD subtype with more severe symptoms (Pierce et al., 2016). Several different eye-tracking paradigms that can be used in infancy have been developed and studied extensively. This study focuses on two different paradigms that measure saccadic reaction time and attentional preferences for faces over non-faces and emotional facial expressions over neutral facial expressions.

### *1.2.1 Oculomotor speed in infancy - saccadic reaction time*

Orienting visual attention is dependent on both visual speed and regulation of processes of saccade initiation (Rommelse, Van der Stigchel, & Sergeant, 2008). Oculomotor speed can be studied by tracking sequences of saccadic eye movements (or saccades). Saccades are rapid eye movements that move the point of regard from one position in space to another. We use saccades when we move our gaze around our complex visual environment reacting to external cues or actively searching for information relevant to our current motivation and goals (Haishi, Okuzumi, & Kokubun, 2011; Kennard, 2002). Saccadic reaction time (SRT), measured by automated eye-tracking, is one of the primary variables that reflect the properties of visuospatial processing (Haishi et al., 2011). Saccade latency is, for instance, regarded as a measure of the speed of visual processing, whereas variability in latency indexes the consistency and accuracy of saccade initiation.

During development saccadic reaction times and saccadic regulation changes. Saccadic reaction times decrease during childhood developing fast in infancy and slowing down around nine months of age (Kenward et al., 2017) and reaching adult speed around 12 years of age (Alahyane et al., 2016; Fukushima, Hatta, & Fukushima, 2000) . Children also show bigger standard deviations than adults in SRT measurements (Doettl & McCaslin, 2018) .

Saccade length, measured by amplitude relative to target location, is shorter in children when compared to adults (Alahyane et al., 2016). The saccadic amplitudes in infants and toddlers increase with training showing that learning is able to affect early saccadic processing (Alahyane et al., 2016). The regulation of saccadic speed and accuracy in infancy and childhood is affected by both environmental factors, such as learning processes, and neural development and maturation (Kenward et al., 2017).

SRTs are also used as a measure of the effects of prenatal alcohol exposure and can differentiate those with fetal alcohol spectrum disorder (FASD) from typically developing controls (Green et al., 2009; Paolozza, Munn, Munoz, & Reynolds, 2015) . FASD children have been shown to have longer SRTs and higher variability in SRT tasks (Green et al., 2009). Interestingly there is a gender effect on SRTs in FASD children. FASD girls have longer saccadic reaction times while FASD boys show a deficit in accuracy, indicating that gender differences in SRTs should be considered (Paolozza et al., 2015).

SRT measurements have been used to predict if the child will be diagnosed with ASD. Elison et al. (2013) conducted a longitudinal study on 97 children that underwent eye-tracking at seven months and a clinical assessment at 25 months, comparable to the experimental setup in this study. Sixteen of the children in the study of Elison et al. (2013) were high-familial-risk children who met ASD criteria at 25 months, 40 were high-familial-risk children who didn't meet ASD criteria and 41 were low-risk infants. Elison et al. (2013) found longer SRTs in seven months olds later diagnosed with ASD compared to both other groups. The study concludes that longer SRTs may be a prodromal feature of ASD that could be used to earlier identify high-risk individuals that will meet diagnostic criteria later.

Taken together SRTs show developmental profiles that can reliably be measured by eye-tracking during infancy. SRT measurements have been successfully used to distinguish different clinical groups. SRTs could be seen as a general marker of development with shorter SRTs being associated with beneficial outcomes later in life.

### *1.2.2. Attentional bias towards faces during development*

Attentional bias, the tendency to favor some stimuli compared with others, is a mean for the infant to direct attention to salient stimuli that foster development. Favoring specific stimuli over others in the environment requires more self-regulation than automatically orienting towards stimuli. It requires the ability to inhibit automatic responses to some stimuli in favor of more salient ones. Attentional inhibition develops during the first year of life. The spontaneous tendency to look at others' faces is a well-documented hallmark of infants' behavior observed across different cultural settings (Pyykko, Ashorn, Ashorn, Niehaus, & Leppanen, 2019) having importance for cognitive adaptation that ensures infants' engagement in developmentally crucial facial interactions with caregivers (Leppanen, 2016). The preference for faces in four to twelve month old infants can be measured as relatively longer dwell times to faces compared to other visual objects (Leppanen et al., 2011; Peltola et al., 2018) or biased orientation to faces amongst multiple competing objects (Gluckman & Johnson, 2013).

Extensive research has shown that during development, specific attentional biases for faces emerge and in some cases disappear later across infancy and early childhood (reviewed in (Reynolds & Roth, 2018) . Newborns show attentional biases generalized to face-like patterns, such as top-heavy inverse triangles (Valenza, Simion, Cassia, & Umiltà , 1996) , although this preference no longer exists at three months of age (Chien, 2011). Other emerging facial attentional biases during development include a preference to own mother's face (e.g. Pascalis et al., 1995), a preference for faces with direct gaze (Farroni, Menon, & Johnson, 2006) , a preference for women over men (Quinn, Yahr, Kuhn, Slater, & Pascalils, 2002) and a preference for own-race faces compared to other-race faces (Sangrigoli & De Schonen, 2004). Many of these preferences emerge around three months and get attenuated around six to nine months (reviewed in Reynolds & Roth, 2018). Girls spend longer times looking at faces compared to boys but the face preference is evident regardless of gender (Gluckman & Johnson, 2013). These responses to faces are highly malleable and can change even with limited experience (Reynolds & Roth, 2018). This is demonstrated by examples that show that the preference for women over male faces can be reversed if the primary caregiver is a male instead of female (Quinn et al., 2002). The own-race preference is also easily extinguished by exposure to other-race faces regularly (Anzures et al., 2012; Bar-Haim, Ziv, Lamy, & Hodes, 2006).

Although the preference for faces exists already in newborns research findings indicate that the preference for faces compared to other non-social stimuli is getting more attenuated between four and eight months (Bahrick, Lickliter, & Castellanos, 2013; Frank, Vul, & Johnson, 2009; Kwon, Setoodehnia, Baek, Luck, & Oakes, 2016). At this developmental time point infants' preference to look at faces is also consistent across different types of face stimuli, such as individual face pictures and faces in natural scenes (Gillespie-Smith et al., 2016). A marked reduction in face preference occurs between ages seven and 24 months, although it still is evident at 24 months (Peltola et al., 2018) indicating that the attention to faces is at its peak around six to twelve months of age.

The underlying significance of the well-documented bias to attend to faces for its hypothesized role in early social development has only recently begun to be explored. One line of studies focuses on face preference in ASD where the diagnostic criteria include social impairment. Studies show that toddlers with ASD show less preference for faces compared to toddlers with other developmental delays or typically developing peers (Chawarska, Volkmar, & Klin, 2010) . Less face preference is also seen in ASD high-risk infants (that have a sibling with a confirmed diagnosis) when compared to low-risk infants (that have typically developing siblings, Droucker, Curtin, & Vouloumanos, 2013). A more pronounced preference for faces also predicts better expressive language at 18 months in the high-risk infants (Droucker et al., 2013). These results suggest that face-processing differences in toddlers with ASD may, at least partly, underlie deficits in later language development and social communication (Droucker et al., 2013).

Studies on the role of face preference for the social development in typically developing children are also emerging. One study explored the possible link between social and emotional impairment in toddlers and lower face preference in infancy. In a population based sample of 213 participants the study found that lower face preference for direct-gaze, measured by eye-tracking at five weeks, significantly predicted higher callous-unemotional traits (disregard of others' distress and lack of empathy) assessed by parental questionnaires at 25 months (Bedford et al., 2015). Another study on a population-based sample (N=100-138) examined the association of face preference at seven months old with various measures of social development at both 24 and 48 months (Peltola et al., 2018). The results show that bigger attention to faces at seven months is related to more frequent helping behavior at 24 months and reduced callous-unemotional traits at 48 months but on the other hand is not associated with emotion understanding or mentalizing abilities at 48 months of age (Peltola et al., 2018). Taken together there is emerging evidence on more pronounced attentional preference for faces being associated with beneficial social development during toddlerhood.

### *1.2.3 Attentional bias towards emotional faces during development*

In addition to a preference for faces differences in attentional biases between different emotional facial expressions is also seen during infancy. This is hypothesized to be another developmental marker with a role in emotional development (Leppanen & Nelson, 2009). Being able to distinguish emotional facial expressions is a prerequisite for recognition of emotions in one-selves and others. Interpreting emotional cues is important for the process of learning through the emotional responses of caregivers as this indicates their individual feelings and intentions (Leppanen, 2016). For the pre-verbal infant learning to produce appropriate facial expressions is also a central way of communication.

Developmentally the time course of discriminating between different emotional facial expressions follows that of the attentional bias to faces discussed earlier. Infants categorically discriminate between different emotional facial expressions within the first six months (reviewed in Leppanen & Nelson, 2009). Research shows that the development of discriminating between different facial expressions is a dynamic process during infancy, comparable to that of the overall preference for faces. Newborns show a preference for happy over neutral faces (Farroni, Menon, Rigato, & Johnson, 2007). An attentional bias for fearful over happy and neutral faces starts around five months when this preference can be seen using dynamic face stimuli (Heck, Hock, White, Jubran, & Bhatt, 2016; Heck, Hock, White, Jubran, & Bhatt, 2017) and is particularly robust and much studied at seven months when it can be seen also when using pictures of static faces (e.g. Peltola, Leppanen, Maki, & Hietanen, 2009; Peltola, Leppanen, & Hietanen, 2011, Leppanen, Cataldo, Bosquet Enlow, & Nelson, 2018). This attentional bias is noted to coincide with mobility and is hypothesized to underline the importance for infants to interpret caregiver's warnings of threat (Leppanen & Nelson, 2009) . This hypothesis is supported by the observation that infants are specifically more sensitive to fearful faces that refer toward something in the environment than fearful faces with direct eye gaze (Hoehl & Striano, 2010). The attentional bias for fearful faces is followed by biases for other emotional expressions such as a bias for angry faces (Burris, Barry-Anwar, & Rivera, 2017). The particularly strong attentional bias towards fearful faces at seven months declines toward 24 months (Peltola et al., 2018) and can be modified by environmental factors such as mothers' prenatal anxiety symptoms (Kataja et al., 2019) and mothers' pre- or postnatal depressive symptoms (Forssman et al., 2014; Kataja et al., 2018) as well as known genetic risk-factors for depression (Forssman et al., 2014).

To my knowledge there are only a few longitudinal studies on the attentional preference for emotional stimuli in infancy and later outcomes of socio-emotional development. A cohort study on 73 typically developing children found heightened attention to fearful faces at seven months leading to increased odds of secure attachment to the mother at the age of 14 months (Peltola et al., 2020), suggesting that patterns of secure and insecure infant attachment are related to early-emerging differences in the perceptual processing of facial emotions. Another study on 64 typically developing children found that infants who showed heightened initial attention to fearful faces (measured by a prolonged first look) followed by greater disengagement of fearful faces (measured by reduced attentional bias over 15 seconds) displayed greater prosocial behavior at 14 months of age in tasks designed to measure altruistic behaviors (Grossmann et al., 2018).

Considerable research links threat-related attention biases, such as a bias toward fearful faces, to anxiety in adults (Armstrong & Olatunji, 2012) . There is evidence for a similar association in school-aged children with anxious children showing a greater bias for threat-related stimuli than control children (reviewed in Dudeney, Sharpe, & Hunt, 2015). This association is more prominent for social anxiety and school phobia symptoms and is positively correlated with the severity of anxiety symptoms (Abend et al., 2018). To my knowledge possible associations of attentional biases towards fearful faces in infants and later anxiety symptoms have not been studied. The bias for fearful emotional faces seen linked to anxiety symptoms in both typically developing children and adults can not be seen in children with ASD, suggesting that this sub-population possibly has different cognitive correlates for anxiety (Hollocks, Ozsivadjian, Matthews, Howlin, & Simonoff, 2013) .

There is emerging evidence on the importance of attentional biases towards emotional faces in particular in infancy for socio-emotional development. However findings on the developmental outcomes associated with the attentional bias for fearful faces over other facial expressions show different outcomes linking the phenomenon to both beneficial socio-emotional outcomes as well as anxiety symptoms.  Understanding and interpreting these associations still needs a lot of research on the importance of this attentional marker at different developmental stages. Longitudinal studies give much needed understanding on the importance of these well documented and described developmental milestones.

# 2. AIMS OF THIS STUDY AND HYPOTHESIS

The goal of this study is to explore the potential of recognizing risk factors early in development based on infants' individual eye-tracking performance profiles in two different tasks; a saccadic reaction time task and a task measuring face preference. This study focuses on adaptive behaviour as a developmental outcome. Adaptive behaviour, a clinically relevant construct, is measured at two years of age by a parent-filled questionnaire.

This study utilized newly developed eye-tracking indexes from the Toibilas-project, developed with the aim to find clinically meaningful individual-level predictors of subsequent development. The indexes used in this study measure several standardized features of SRTs, behavioural discrimination of faces versus non-faces as well as emotional (happy and fearful) versus neutral facial expressions.

Furthermore three groups based on the individual behavioural attentional tendencies have been identified in the Toibilas-project based on several combined SRT features. The association of these groups and adaptive behaviour scores at two years of age are explored.

Associations between SRT-measures, behavioural attentional tendency groups and attentional biases for faces and emotional faces and adaptive behaviour outcomes were explored in a sample with healthy controls as well as a high-risk group to increase variability of the sample.

Research questions:

1) Are standardized SRT features, as measured by eye-tracking at seven months, associated with adaptive behaviour assessed by a parent-filled questionnaire at two years?
   Hypothesis: Shorter SRTs are associated with better adaptive behaviour scores at two years of age.
2) Is behavioural discrimination between faces and non-faces, measured by eye-tracking at seven months, associated with adaptive behaviour assessed by a parent-filled questionnaire at two years?
   Hypothesis: A bigger attentional difference in looking times between facial and non-facial stimuli is associated with better adaptive behaviour scores at two years of age.
3) Does behavioural discrimination between emotional and neutral facial expressions, measured by eye-tracking at seven months, predict adaptive behaviour assessed by a parent-filled questionnaire at two years?

No exact hypothesis, an explorative analysis is done.

4) Are behavioural attentional tendency groups, identified by combining eye-tracking SRT-measures at seven months, associated with adaptive behaviour, assessed by a parent-filled questionnaire at two years?

   No exact hypothesis, an explorative analysis is done.

## 3. MATERIAL AND METHODS

### 3.1 Participants

The final analysis of this study included 45 or 44 infants (boys n=28, girls n=17), depending on the analysis (see Figure 1). The participants included both healthy term children (n=26) and children representing a high-risk group that had been committed to the neonate intensive care unit after birth for any reason (e.g. pre-terms or asphyxia during labour, n=19). The high-risk group included eleven preterm infants. The healthy term children were recruited by ordering contact information for a sample from the Population Registration Center. The families with children in the right age and geographical range were informed about the study and given a chance to participate. Inclusion criteria for the healthy term children were full term birth, no complications during pregnancy and birth, healthy as new-born and no need for more intensive follow-up during neonatal period or early infancy. The high-risk group was recruited at the Helsinki University Hospital neonatal policlinic seven where all infants of the right age range were informed about the study and given a chance to participate. Inclusion criteria for the high-risk group were that the child received intensive care after birth. The high-risk group of children were included in this dataset with the aim of testing the applicability of the indexes used in both low-risk and high-risk groups as well as expanding the variability of the group and therefore increasing the probability of detecting clinically meaningful biomarkers from the eye-tracking experiment.

Of the 143 families that expressed interest in participating in the Toibilas-study106 participated in eye-tracking measurements at seven months (see Figure 1). Technically acceptable eye-tracking data was obtained from 57 infants (see Figure 1). Two infants were too fussy at the recording session to be able to finish the recording. The remaining missing data is due to either technical difficulties (n=35) or it is unclear if the child was too fussy or missing is due to technical difficulties (n=11). The seemingly big number of technically unsuccessful eye-tracking measurements was partly due to technical difficulties in setting up and optimizing the eye-tracking measurement. However, this number of unsuccessful measurements with infants of this age is not unheard of (Leppanen et al., 2018). Retaining a successful eye-tracking result was not dependent on the if the infant belonged to the high risk group ($X^2$ (1, N=106) = .46, $p > .05$), whether the infant was born pre- or full-tem ($X^2$ (1, N= 106) = 1.54, $p > .05$) or the gender of the infant ($X^2$ (1, N = 106) = 1.65, $p > .05$ ) .

The families were asked to return for a follow-up at 24 months and asked to fill in the Adaptive Behaviour Questionnaire (ABQ) as part of a standard neuropsychological assessment using the

Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III, 3rd edition). The families with infants that had a successful eye-tracking measurement were more likely to return for the follow-up study ($X^2$ (1, N = 106) = 14.61, $p < .001$). The probability of returning the ABQ at 24 months was not affected by the gender of the infant ($X^2$ (1, N = 106) = 0.26, p = .61), if the infant belonged to the high-risk group ($X^2$ (1, N = 106) = 0.72, p = .40) or if the infant was born preterm ($X^2$ (1, N= 106) = 2.37, p = .12).

Of the 57 infants with successful eye-tracking 45 returned the ABQ at 24 months rendering N = 45 or 44 depending on analysis (see Figure 1).

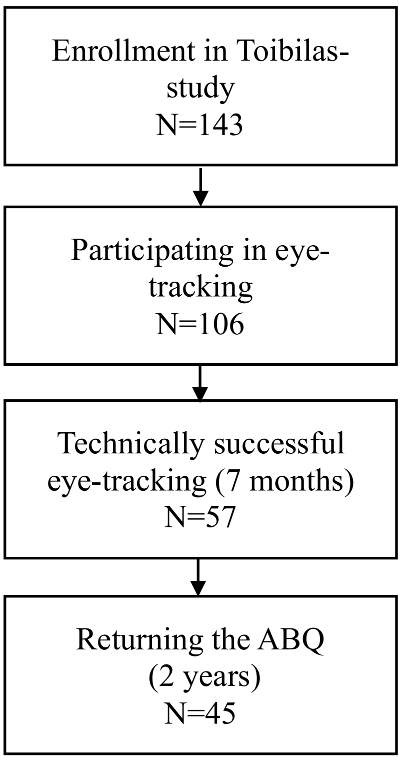


Figure 1. Formation of the final sample.

The participation was voluntary and the research study protocol was approved by Helsinki University Hospital (HUH). Ethical consent came from the HUH Ethics Committee for gynaecology and obstetrics, paediatrics and psychiatry. Written informed consent was given by the parents of the participants before the start of the study.

## 3.2 Eye tracking measurements

### *3.2.1. Experimental procedure*

Eye-tracking experiments were done between 2/2015 and 1/2017 in Helsinki University Hospital at seven months of age (*M* = 7.46 months, *SD* = 0.32, between 6.63 - 7.93 months), corrected age for pre-terms as this is the standard procedure up to two years of age in neurocognitive experiments. Infants were placed in a baby björn carrier and were sitting in their caregiver's lap during the eye-tracking measurement at 50-60 cm from the screen (24" ASUS VE247, 60 Hz refresh rate and 2 ms response time, resolution 1920x1080). The caregiver was instructed to keep their eye-gaze away from the screen. Eye movements were recorded using a Tobiix60 or x120 eye-tracker and Data Recording Open-Source Platform (https://github.com/infant-cognition-tampere/drop).
Prior to the actual test paradigm a calibration was performed. A visual stimulus, an animated object, was shown in the centre of the screen and in the four corners successively. The task did not proceed before the infant had fixated on the stimulus. Fixation at the different locations was verified by use of an automated calculation using an error vector. If fixations at all the indicated locations was unsuccessful a second calibration trial was done after that the actual experiment was started regardless if all locations had successful fixations or not. The calibration was successful, according to laboratory notes, in 88 measurements (of which 53 measurements gave usable data), partially successful in eight measurements (three usable measurements) and unsuccessful in eight measurements (one usable measurement), data on successful calibration was missing in two cases. Calibration being unsuccessful significantly affected if the eye-tracking measurement is successful ($X^2$ (1, N = 104) = 7.79, p = .02) with successful calibration increasing the probability of having a successful measurement. Unsuccessful calibration could be due to either technical difficulties or the infant behaviour e.g. not orienting towards the screen or fixating the stimuli.

Two different paradigms were used for the eye-tracking measurements: an SRT gap-paradigm (saccadic reaction time, described in more detail in section 3.2.2) and a FACE overlap-paradigm (as described in Leppänen 2011). 12 trials were recorded for the SRT gap-paradigm divided into three different sessions and 16 trials divided into two sessions for the FACE overlap-paradigm. The SRT gap and FACE overlap-paradigm sessions alternated during the recording. Between the sessions the infant was allowed to watch short movies that kept the interest toward the screen.

Testing was paused if the infant became fussy or tired and was terminated if the experimenter (consulting the parent) determined that continuing the testing would have been too distressing for the infant. The duration of the whole experimental procedure was approximately 15-20 minutes.

### *3.2.2 SRT gap-paradigm*

In the SRT gap-paradigm a fixation stimulus, an animated checkerboard accompanied with a sound, is shown in the middle of the screen to attract the infant's attention and eye gaze (see Figure 2). The fixation stimulus is shown in the middle of the screen until the infant has fixated on it for 500 ms after which the fixation stimulus disappears and a target stimulus, visually identical but without sound, appears in one of the four corners of the screen. When the child moves his or her gaze to the target stimulus the checkerboard turns into a reward stimulus, which in this case is a smiling face.

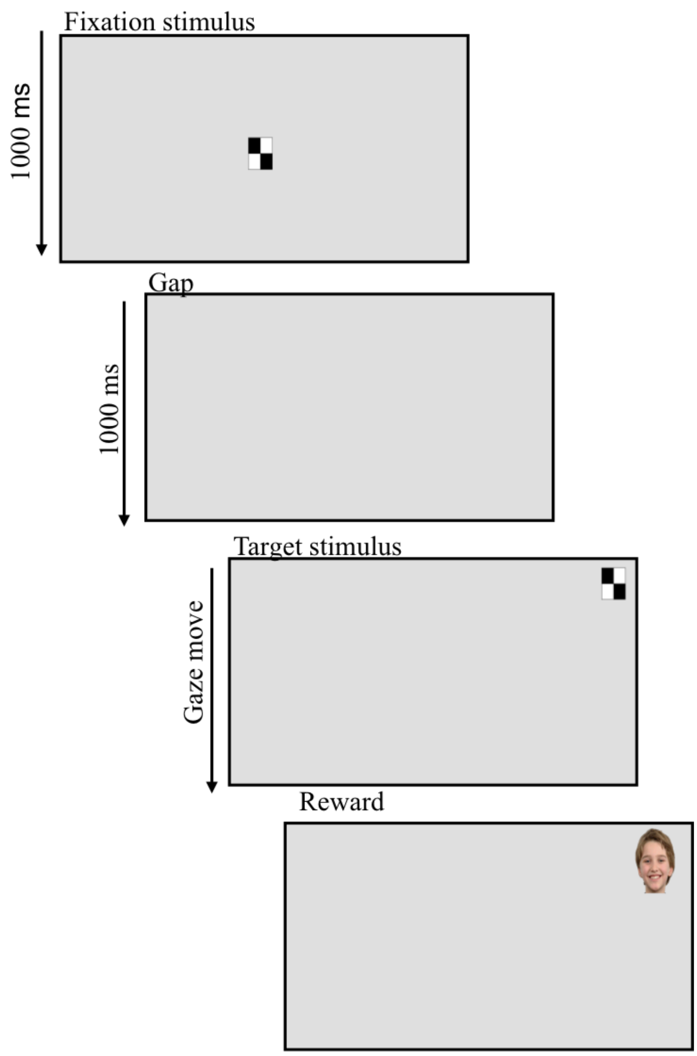


Figure 2. The SRT gap-paradigm.

### *3.2.3 The FACE overlap-paradigm*

In the FACE overlap-paradigm a fixation stimulus, a cross, is first shown in the middle of the screen, until the infant fixated on it, followed by a central stimulus (see Figure 3). The central stimuli were two different woman faces presented with three different emotional expressions or an unrecognizable phase scrambled face (Leppanen et al., 2011). The emotional expressions were neutral, happy and fear, validated to signal the intended emotions by a group of adult raters (see Peltola, Leppanen, Palokangas, & Hietanen, 2008 for further details).

During the measurement the central stimulus was shown for a period of 4000 ms. After 1000 ms a competing peripheral stimulus, a checker-board or black and white balls, appeared on the right or left side of the target stimulus and remained visible for the last 3000 ms of the trial (see Figure 3).

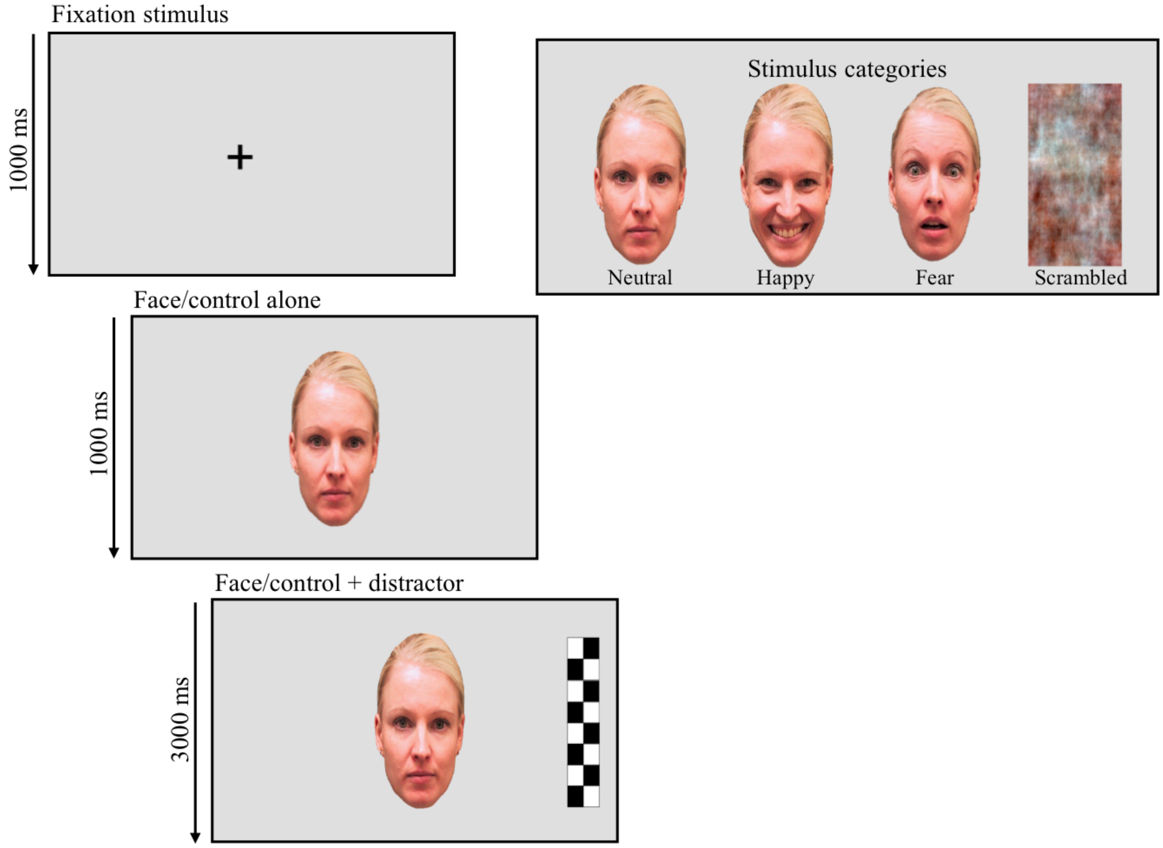


Figure 3. The FACE overlap-paradigm.

### *3.2.4 Analysis of eye-tracking raw data*

The hardware used for recording the eye movements was an automated screen based eye-tracking system Tobii pro-X3-120 with external processing unit. Tobii eye-tracker provides e.g. coordinates for gaze points based on recorded infrared reflection patterns, image processing and 3D-eye ball models.  Validity estimates are also provided on a scale from zero to four for both eyes and every time point. Only data with good validity for gaze recognition (values zero to one) was used according to the manufacturer's recommendations. After this, the eye-tracker was pre-processed using ICL Matlab (for further details see (Leppanen, Forssman, Kaatiala, Yrttiaho, & Wass, 2015) . Data from both eyes was combined for every time point. If data from one eye was not valid, the data from the other eye was used. Missing or non-valid (combined) data points were interpolated with previous valid data point and the data was then median filtered with length of seven data points. The data was cut into the trial length and every trial was analysed separately. If there was a continuous time period over 200 ms of invalid data the trial was rejected. The data was cut into central area of interest (central AOI) and peripheral AOIs. The lower limit for saccadic response was set for 150 ms and higher limit to 1000 ms. The trial was rejected if gaze shift occurred during the invalid period. The trial was also rejected if the fixation to the central stimulus was unreliable (proportion of successfully tracked fixation inside central AOI was less than 0.7) after the gaze had entered to the central area for the first time and the trial had begun. For the trials with gaze shift, only the trials where the gaze inside peripheral AOI was over 750 ms (SRT gap-paradigm) or 1000 ms (FACE overlap-paradigm) were accepted. For FACE overlap-paradigm the proportion of gaze inside central AOI was calculated for the time period starting from the appearance of the peripheral target up to the successful gaze shift. If a child did not shift gaze, then the proportion was 1.

### *3.2.5 Indexes from the SRT gap-paradigm and behavioural attentional tendency groups*

Three different measures describing the distribution of the SRTs were chosen all based on cumulative fixations time (in ms) on the fixation stimulus after the appearance of the target stimulus: the median of the saccadic response times (SRTmed), average of the 50 % of fastest reaction times (SRT50%, corrected for SRTmed to avoid multicolinearity) and the 90$^{th}$ percentile point of the reaction times (SRT90p). All indexes were standardized based on control group values. Combining data from all three SRT indexes every child was grouped into one of three groups according to their behavioural attentional tendency; fast (n = 10), average (n = 30) and slow (n = 17) responders. The grouping was done using cluster analysis in the Toibilas project, BABA-center (unpublished results). Gender significantly affected the behavioural attentional tendency grouping of the infants ($X^2$ (1, N = 57) = 6.01, p = .05). Girls were more evenly distributed to the different groups (seven fast, eight average and seven slow) than boys (three fast, 22 average and ten slow). Belonging to the high-risk group ($X^2$ (2, N =57) = 0.84, p =.66) or pre-term birth ($X^2$ (2, N = 57) = 0.38, p = .83) did not affect the identified group identity of the infant.

### *3.2.6 Indexes from the FACE overlap-paradigm*

In the FACE overlap-paradigm the considered measure from each trial is the time (in ms) the infant fixates their gaze on the central stimulus after the distractor has appeared on either side. Indexes from the FACE overlap-paradigm were extracted combining data over different facial expressions. The indexes considered from the FACE overlap-paradigm is the difference of mean fixation time on the central stimulus between facial and non-facial stimuli (FACE) and the difference of mean fixation time on the central stimulus between neutral facial expressions and emotional (either happy or fearful) facial expressions (EMO). The indexes from the FACE overlap-paradigm were adjusted to average fixation times of the individual i.e. they depict differences between conditions. The indexes were standardized against control group values development of the indexes was done in the Toibilas-project, BABA center (unpublished results).

## 3.3 Assessment of adaptive behaviour at two years of age

The adaptive behaviour at 24 months (*M* = 25.51 months, *SD* = 1.26, between 24.10-28.24 months) was measured by The Adaptive Behavior Questionnaire (ABQ), whish is identical to the Adaptive Behavior Assessment System II (ABAS-II) and is developed by Patti L. Harrison and Thomas Oakland. The results from the questionnaires were corrected for prematurity, as applicable, because it has been shown that corrected standardized points better predict outcomes at school age (O'Shea et al., 2018). The ABQ includes ten subscales of 22-27 questions each related to skills in different areas (see Table 1). The ABQ has four domain composite scores that were used as dependent variables in this study; General Adaptive Composite (GAC) and Conceptual, Social and Practical composite domains. GAC is a global score of adaptive behaviour including all of the skill areas as well as motor skills that is not included in any of the domain composites.

Table 1. Skill areas of composite domains of the ABQ.

| Conceptual composite domain | Social composite domain | Practical composite domain |
|---|---|---|
| Communication | Leisure | Self-care |
| Functional academics | Social skills | Home living |
| Self-Direction | | Community use |
| | | Health and safety |

### 3.4 Statistical analysis

All statistical analyses were done using SPSS software version 25. Two different linear models for each adaptive composite score were constructed yielding eight linear models in total. All models included gender, pre-term/full-term status and clinical group (control or high-risk group) as background factors

In model 1 independent effects of the different eye-tracking indexes were observed by constructing multiple linear regression models with each of the four adaptive behaviour composite scores as dependent variables; GAC (N=44), conceptual (N=45), social (N=45) and practical (N=45) composite domains, yielding four model 1 analyses. Independent variables were three eye-tracking indexes from the SRT gap-paradigm; SRTmed (corrected for SRT50% to avoid multicolinearity), SRT 50% and SRT90p, and two indexes from the FACE overlap-paradigm; FACE and EMO along with relevant background factors.

In model 2 associations between adaptive behaviour composite scores and identified behavioural attentional tendency groups were analysed by analysis of covariance (ANCOVA), yielding four model 2 analyses. All ANCOVA models included behavioural attentional tendency groups and two indexes from the FACE overlap-paradigm; FACE and EMO, as independent variables along with relevant background factors. Standardized coefficients for continuous variables were calculated with simple estimation by dividing the standard deviation of the independent variable with the standard deviation of the dependent variable and multiplying the quotient with the raw coefficient. For statistically significant findings on associations between adaptive behaviour scores and attentional behavioural tendency groups analysis of variance was performed including pair-wise comparisons with post-hoc bonferroni correcting for multiple comparisons.

# 4. RESULTS

All results from analyses of model 1 are presented in Table 2 and results from analyses of model 2 are presented in Table 3.

The models predicting GAC found statistically significant association only between FACE and GAC. A larger difference between looking times for facial and non-facial stimuli is associated with higher GAC scores in both models 1 (presented in Table 2) and 2 (presented in Table 3).

The results from analyses predicting conceptual composite domain scores show that FACE had a statistically significant correlation with conceptual composite domain scores in model 1. The association between FACE and conceptual composite domain scores does not reach statistical significance in model 2, where behavioural attentional tendency groups, based on all SRT-indexes are included. In model 2 behavioural attentional tendency groups are statistically significant predictors of conceptual composite domain scores. Analysis of variance confirms an overall difference between behavioural attentional tendency groups ($F(2,42)=3.68$, $p=.03$). Conceptual composite domain score descriptive statistics and pairwise comparisons between groups are presented in Table 4. The difference in conceptual composite domain scores is statistically significant between infants with average and slow behavioural attentional tendencies with infants in the average group getting higher conceptual composite domain scores compared to infants in the slow group. The difference is not statistically significant after bonferroni correction for multiple comparisons.

Table 2. Model 1; Multiple linear regression analyses predicting all four adaptive behaviour composite domain scores with individual eye-tracking indexes and relevant background factors *indicates p<.05.

| | | | β | t | p | F (df1,df2) | p | $R^2$ |
|---|---|---|---|---|---|---|---|---|
| GAC | Background factors | Gender | -.20 | -1.16 | .25 | 1.08 (8,35) | .40 | .20 |
| | | High-risk/control | -.19 | -.89 | .38 | | | |
| | | Preterm/Fullterm | .29 | 1.28 | .21 | | | |
| | Eye-tracking variables | SRTmed | .11 | .63 | .53 | | | |
| | | SRT50% | -.09 | -.54 | .60 | | | |
| | | SRT90p | .01 | .04 | .97 | | | |
| | | FACE | .44 | 2.32 | .03* | | | |
| | | EMO | -.04 | -.20 | .85 | | | |
| Conceptual composite | Background factors | Gender | -.14 | -.89 | .38 | 1.83(8,36) | .10 | .29 |
| | | High-risk/control | .08 | .42 | .677 | | | |
| | | Preterm/Fullterm | -.05 | -.26 | .80 | | | |
| | Eye-tracking variables | SRTmed | .22 | 1.35 | .19 | | | |
| | | SRT50% | -.30 | -1.87 | .07 | | | |
| | | SRT90p | -.02 | -.13 | .90 | | | |
| | | FACE | .36 | 2.16 | .04* | | | |
| | | EMO | -.07 | -.43 | .67 | | | |
| Social composite | Background factors | Gender | .06 | .37 | .71 | 1.36 (8,36) | .25 | .23 |
| | | High-risk/control | -.17 | -.89 | .38 | | | |
| | | Preterm/Fullterm | .17 | .83 | .41 | | | |
| | Eye-tracking variables | SRTmed | .04 | .21 | .83 | | | |
| | | SRT50% | .32 | 1.87 | .07 | | | |
| | | SRT90p | -.21 | -1.19 | .24 | | | |
| | | FACE | .27 | 1.55 | .13 | | | |
| | | EMO | .04 | .23 | .82 | | | |
| Practical composite | Background factors | Gender | -.18 | -1.10 | .29 | 1.38 (8,36) | .24 | .24 |
| | | High-risk/control | -.12 | -.62 | .54 | | | |
| | | Preterm/Fullterm | .41 | 2.00 | .05 | | | |
| | Eye-tracking variables | SRTmed | .07 | .44 | .66 | | | |
| | | SRT50% | -.1 | -.58 | .56 | | | |
| | | SRT90p | -.08 | -.45 | .66 | | | |
| | | FACE | .44 | 2.50 | .02* | | | |
| | | EMO | .03 | .17 | .87 | | | |

Table 3. Model 2; ANCOVA analyses predicting all four adaptive behaviour composite domain scores with behavioural attentional tendency groups, eye-tracking indexes from the FACE overlap-paradigm and relevant background factors. SE is standard error,* indicates p<.05 and °indicates the reference group. Table 3 continues on the following page.

| | | | Coefficient | SE | t | p | F(df1,df2) | p | $R^2$ | Standardized coefficient |
|---|---|---|---|---|---|---|---|---|---|---|
| GAC | | Intercept | 88.81 | 4.77 | 18.63 | <.000 | 1.63 (7,36) | .16 | .24 | |
| | Background factors | Gender, boy | 1.83 | 3.47 | .53 | .60 | | | | |
| | | Gender, girl° | 0 | . | . | . | | | | |
| | | Preterm birth | -3.86 | 4.78 | -.81 | .43 | | | | |
| | | Fullterm birth° | 0 | . | . | . | | | | |
| | | Control | -2.12 | 3.95 | -.54 | .59 | | | | |
| | | High-risk° | 0 | . | . | . | | | | |
| | Behavioral attentional tendency group | Fast | -.87 | 4.70 | -.19 | .85 | | | | |
| | | Average | 4.93 | 3.63 | 1.36 | .18 | | | | |
| | | Slow° | 0 | . | . | . | | | | |
| | Eye-tracking indexes | FACE | 5.04 | 2.44 | 2.07 | .05* | | | | 0.32 |
| | | EMO | -.46 | 1.52 | -.30 | .77 | | | | -0.03 |
| Conceptual composite | | Intercept | 83.13 | 5.11 | 16.26 | <.000 | 2.55 (7,37) | .03* | .33 | |
| | Background factors | Gender, boy | -.37 | 3.83 | -.10 | .92 | | | | |
| | | Gender, girl° | 0 | . | . | . | | | | |
| | | Preterm birth | 5.37 | 5.10 | 1.05 | .30 | | | | |
| | | Fullterm birth° | 0 | . | . | . | | | | |
| | | Control | 3.73 | 4.20 | .89 | .38 | | | | |
| | | High-risk° | 0 | . | . | . | | | | |
| | Behavioral attentional tendency group | Fast | 2.77 | 5.34 | .52 | .61 | | | | |
| | | Average | 10.68 | 3.95 | 2.70 | .01* | | | | |
| | | Slow° | 0 | . | . | . | | | | |
| | Eye-tracking indexes | FACE | 5.20 | 2.61 | 2.00 | .05 | | | | 0.32 |
| | | EMO | -1.15 | 1.73 | -.67 | .51 | | | | -0.09 |

| | | | Coefficient | SE | t | p | F(df1,df2) | p | $R^2$ | Standardized coefficient |
|---|---|---|---|---|---|---|---|---|---|---|
| Social composite | | Intercept | 97.68 | 5.12 | 19.09 | <.000 | 1.20 (7,37) | .33 | .18 | |
| | Background factors | Gender, boy | -.76 | 3.84 | -.20 | .84 | | | | |
| | | Gender, girl° | 0 | . | . | . | | | | |
| | | Preterm birth | -5.60 | 5.10 | -1.10 | .28 | | | | |
| | | Fullterm birth° | 0 | . | . | . | | | | |
| | | Control | -5.39 | 4.20 | -1.28 | .21 | | | | |
| | | High-risk° | 0 | . | . | . | | | | |
| | Behavioral attentional tendency group | Fast | -4.11 | 5.35 | -.77 | .45 | | | | |
| | | Average | 2.26 | 3.96 | .57 | .57 | | | | |
| | | Slow° | 0 | . | . | . | | | | |
| | Eye-tracking indexes | FACE | 4.52 | 2.61 | 1.73 | .09 | | | | 0.28 |
| | | EMO | 1.20 | 1.73 | .70 | .49 | | | | 0.09 |
| Practical composite | | Intercept | 87.72 | 5.16 | 17.01 | <.000 | 1.79 (7,37) | .12 | .25 | |
| | Background factors | Gender, boy | 2.87 | 3.87 | .74 | .46 | | | | |
| | | Gender, girl° | 0 | . | . | . | | | | |
| | | Preterm birth | -10.13 | 5.14 | -1.97 | .06 | | | | |
| | | Fullterm birth° | 0 | . | . | . | | | | |
| | | Control | -2.51 | 4.23 | -.59 | .56 | | | | |
| | | High-risk° | 0 | . | . | . | | | | |
| | Behavioral attentional tendency group | Fast | 1.15 | 5.39 | .21 | .83 | | | | |
| | | Average | 5.29 | 3.99 | 1.33 | .19 | | | | |
| | | Slow° | 0 | . | . | . | | | | |
| | Eye-tracking indexes | FACE | 6.81 | 2.63 | 2.59 | .01* | | | | 0.16 |
| | | EMO | .53 | 1.74 | .31 | .76 | | | | 0.13 |

Table 4. Descriptive statistics of conceptual composite domain scores for attentional behavioural tendency groups and pairwise comparisons between groups. SE is standard error, p adjusted is the bonferroni corrected p-value and *indicates p<.05

| Behavioral attentional tendency group | N | Mean | SE | Pairwise comparison | p | p adjusted |
|---|---|---|---|---|---|---|
| Fast | 9 | 88.33 | 4.64 | Fast vs Average | .06 | .19 |
| | | | | Fast vs slow | .81 | 1.00 |
| Average | 24 | 97.08 | 2.31 | Average vs slow | .02* | .06 |
| Slow | 12 | 87.08 | 3.11 | | | |

The models predicting social composite domain scores found no significant associations between any of the examined variables and the social composite domain scores in either model 1 (Table 2) or model 2 (Table 3).

The models predicting practical composite domain scores found statistically significant association only between FACE and practical composite domain scores. A larger difference between looking times for facial and non-facial stimuli is associated with higher practical domain scores in both models 1 (presented in Table 2) and 2 (presented in Table 3).

The models predicting practical composite domain scores also show an effect for preterm birth almost reaching statistical significance (p=.053 in model 1 and p=.056 in model 2).

# 5. DISCUSSION

In this study newly developed eye-tracking indexes extracted from measurements on seven-month-old infants were explored to investigate their potential for predicting adaptive behaviour at two years of age. In addition to single measures several measures were combined (speed, consistency and accuracy) that resulted in identifying different types of behavioural attentional tendencies. The effects of these tendencies were also explored for their association with adaptive behaviour. Infants' preference for faces compared to non-facial stimuli, measured by eye-tracking, was associated with overall adaptive behaviour scores and practical composite domain scores and showed a trend towards association with conceptual composite domain scores. A bigger attentional difference between faces and non-facial stimuli is associated with better adaptive behaviour at two years of age. The identified behavioural attentional tendency group of the infant at seven months of age predicted adaptive behaviour scores when considering the conceptual composite domain of adaptive behaviour at two years of age.

## 5.1 Associations between attentional markers of SRT in infancy and toddler age adaptive behaviour

Like many predictive markers of early childhood development, also the SRT- indexes used in the present study suffer from unspecificity, as saccadic reaction times are associated with many different diagnoses and later outcomes (Elison et al., 2013; Green et al., 2009). The same is true for adaptive behaviour that was used as the outcome measure in the present study (Santens et al., 2020). Therefore several different factors need to be taken into account identifying groups characterized by combinations of attentional tendencies to be able to interpret results that are meaningful on the individual level. This principle was tested in the Toibilas-project by combining data from different SRT measures and identifying groups of infants characterized by their behavioural attentional tendencies. Identified groups show differences of the conceptual composite domain scores of adaptive behaviour at two years of age. The results show some support for the proof-of principle of grouping infants using measures that traditionally are seen as measures of cognitive processes. In temperament and personality research grouping individuals based on several characteristics has a long tradition while the potential of a similar approach in cognitive research hasn't been explored much.

Statistically significant associations between behavioural attentional tendency groups and adaptive behaviour could only be found for the conceptual composite domain scores. The conceptual composite domain consists of questions from three skill areas: communication, functional academics and self-direction. Many of the questions require language skills (understanding verbal instructions and being able to verbally communicate) but also other cognitive skills as well as executive functions. The conceptual composite domain could be hypothesized to measure the appropriate use of cognitive skills in every day situations. It would be interesting to see whether behavioural attentional tendency groups that showed associations with the conceptual composite domain show correlations with cognitive skills at the same time point. This is studied in the Toibilas-project.

Earlier research findings suggest that faster visual reaction times are associated with clinically beneficial outcomes such as lower risk for later ASD diagnosis in a high-risk population (Elison et al., 2013), higher IQ in ID (Haishi et al., 2011) and being a marker of FASD (Green et al., 2009; Paolozza et al., 2015). In this limited sample saccadic reaction time measures showed significant associations with adaptive behaviour conceptual scores when different measures were combined, but associations between single SRT-indexes measuring speed, consistency and accuracy of SRTs did not have any significant associations with adaptive behaviour scores, contrary to the hypothesis.

### 5.2 Associations between attentional markers of face preference in infancy and toddler age adaptive behaviour

Attentional bias for faces predicted adaptive behaviour scores, overall adaptive behaviour scores as well as practical composite domain scores and conceptual composite domain scores in one of the two linear models. This finding confirmed the hypothesis that a bigger attentional preference for faces is associated with better adaptive behaviour and supports the importance of face preference for socio-emotional development since adaptive behaviour and self-regulation is closely related to socio-emotional development. Surprisingly no effect of face preference could be seen with regards to the social composite domain score in this study. Earlier findings show that a bigger attentional bias for faces in infancy correlates with reduced callous-unemotional traits (Bedford et al., 2015) and more frequent helping in toddlers in the general population (Peltola et al., 2018) as well as better language development in ASD (Droucker et al., 2013) supporting the role of face preference in socio-emotional development.

This study did not find any association between the ability to differentiate between emotional and neutral facial expressions at seven months of age and adaptive behaviour scores at two years. It is possible that this is due in part to the fact that attentional biases are smaller within stimulus categories (faces) than between categories (faces-non-faces, Gluckman & Johnson, 2013) . No hypothesis was set for the association between attentional bias for emotional facial expression and adaptive behaviour since results from earlier research has been mixed. Studies have shown that heightened attention towards fearful facial expressions is associated with both adverse (anxiety disorders, (Abend et al., 2018; Dudeney et al., 2015) and good outcomes (secure attachment, (Peltola et al., 2018).

Pervious studies have used differences between fearful facial expressions and non-faces (Leppanen et al., 2018) or fearful and neutral faces (Heck et al., 2016; Hoehl & Striano, 2010) . In this study the difference between attention to neutral and emotional, both fearful and happy expressions, was considered. This might have led to smaller observed differences between individuals. There is some evidence that attending preferentially to emotional stimuli across valences, in contrast to attentional preference for only negative emotional stimuli could be an important measure, since it is associated with depressive and anxiety symptoms in young adults (Garcia, Francis, Tone, & Tully, 2019) .

### 5.3 Behavioural attentional markers as a tool for predicting developmental outcomes and as intervention targets

This study aimed to use --tracking indexes derived from measurements at seven months of age for predicting behavioural outcomes at two years of age. Eye tracking in infancy has previously been found to be useful as a tool for predicting later outcomes in clinical sub populations as well as typically developing children. One example is the possibility of identifying ASD high-risk infants that later fulfil diagnostic criteria for ASD by their tendency to show longer SRTs (Elison et al., 2013). Developmental trajectories have also been identified in ASD using eye-tracking showing that preferential looking to the eyes is present in two-month-old babies later diagnosed with autism spectrum disorder but is in decline between two and six months (Jones, W. & Klin, 2013) . In typically developing children infant's increased attention measured both neurally and behaviourally at ten months is associated with better emotional control at three years of age (Perry, N. B., Swingler, Calkins, & Bell, 2016) and visual tracking in infancy correlates with neurodevelopment at three years old (Kaul et al., 2016). This study supports the hypothesis that specific eye-tracking measurements in infancy could be useful also when predicting adaptive behaviour, an outcome measure not studied before to my knowledge.

Early recognition of risk factors associated with later development is important for implementing earlier interventions. There are some preliminary promising studies on early interventions targeting attentional development. Attentional control, including SRTs, can be altered in 11 month-old typically developing children with a relatively short structural training procedure (Wass, S., Porayska-Pomsta, & Johnson, 2011) , studies on the feasibility on using similar strategies with very preterm infants are ongoing (Perra et al., 2020). This study found infant facial preference to be associated with later developmental outcomes indicating that facial preference could be investigated as a potential intervention target in infants. It has to be noted that results in this study should be repeated and studied further before possible interventions could be considered.

### 5.4 Adaptive behaviour as a developmental outcome measure

When considering results on attentional measures and later outcomes it has to be emphasized that attentional tendencies are influenced both by innate and environmental factors. In this study adaptive behaviour is measured by a parent-filled questionnaire rendering the outcome measure to specifically reflect interaction between the child and the parent. It has been shown that parental interaction influences attentional physiology and behaviour during the first year of life with mothers' intrusiveness at five months having negative effects on attention development at ten months (Swingler, Perry, Calkins, & Bell, 2017) . It has also been shown that mothers' depressive symptoms in infancy affects executive function at three years of age, showing a direct relationship between parental behaviour and later self-regulation (Gueron-Sela et al., 2018). Other environmental factors also play a role in how attentional abilities affect self-regulation indicated by the fact that attentional abilities seem to mediate effects of early-life socio-economic adversities with multiple aspects of later self-regulation (Brandes-Aitken, Braren, Swingler, Voegtline, & Blair, 2019) . These studies indicate that reciprocal interactions between individual characteristics and parenting behaviours influence a child's regulatory behaviours over time (McClelland & Cameron, 2011) from very early on.

However using parental questionnaires for measuring adaptive behaviour has many limitations. Questionnaires are always a subjective measure depending on the specific informant, which can lead to considerable variance in scores for children with equal skills. Furthermore some parents might be inclined to answer favourably when their child is being assessed.

### 5.5 Limitations of this study

Limitations of this study include a relatively small number of participants. This is also reflected in the number of infants in the different reaction-type groups being relatively small. Small data-sets might lead to increased probability of both getting statistically significant and clinically insignificant results by chance (false positives) as well as not being able to detect more subtle but clinically relevant differences. However, if significant results can be seen in a smaller sample, that are true positives, the effect size of the phenomenon is likely to be big and therefore have a better potential of being clinically significant.

Eye-tracking, like all methods, has several limitations and sources of errors. The data quality obtained from eye-tracking is usually better with increasing age (Wass, Sam, 2016) leading to difficulties in obtaining good-quality data from infants which might explain some of the seemingly big number of unsuccessful eye-tracking measurements. Studying infants with eye-tracking is dependent on many parameters (specifics of processing the raw data) chosen by the investigator. Results obtained from the measurements are dependent on the chosen parameters, which underlines the importance of the chosen parameters for being able to include as many measurements as possible while discarding erroneous data.

Eye-tracking data is always limited by the paradigms chosen and their ecological validity. One limitation of the paradigms used in this study is the use of static faces in the FACE overlap-paradigm since this has been shown to affect results (Heck et al., 2016; Heck et al., 2017) .

One limitation in this study is that adaptive behaviour was assessed using only one informant rendering the results dependent on the subjective interpretation of one person. The definition of adaptive behaviour includes that the construct measures the interaction between the individual, their skills and the demands entailed by the environment. At two years of age the parents form a significant part of the environment that the child is living in and are therefore relevant informers on how well the child can meet the standards of the environment. Using multiple informants would increase the reliability of using questionnaire-data.

### 5.6 Conclusions

This has been a partially data-driven study on a relatively small data-set with the aim to examine possible associations of behavioural attentional markers in infancy with adaptive behaviour in toddler-age. The results show preliminary promise for the utility of using attentional bias for faces for predicting later adaptive behaviour and self-regulation.

SRT measures were associated specifically with the conceptual composite domain scores of adaptive behaviour possibly connected to cognitive abilities, which should be studied further. The results show some promise for the importance of identifying behavioural attentional tendencies of the individual infant since this is associated with some of later adaptive behaviour outcomes. Identifying attentional tendency groups based on several SRT-measures should be repeated in an independent sample to elucidate the generalization of this kind of identification in other samples.

Much more research is needed to investigate the usefulness of the eye-tracking indexes used in this study regarding possible predictive value for later adaptive behaviour. One line of research could be the use of these indexes and behavioural attentional tendency groups for recognizing risk-factors for specific clinical groups. Studying associations of these attentional markers with different developmental outcomes, like cognitive development, would also be interesting. Taken together this study found associations between behavioural attentional tendency groups and attentional bias for faces in infancy and adaptive behaviour at two years of age raising questions of the usefulness of these attentional markers for predicting different developmental outcomes.

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