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Running head: parent-infant interaction and autism

Parent-child interaction during the first year of life in infants at elevated likelihood of autism spectrum disorder

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## Abstract

Autism spectrum disorder (ASD) likely emerges from a complex interaction between pre-existing neurodevelopmental vulnerabilities and the environment. The interaction with parents forms a key aspect of an infant's social environment, but few prospective studies of infants at elevated likelihood (EL) for ASD (who have an older sibling with ASD) have examined parent-child interactions in the first year of life. As part of a European multisite network, parent-child dyads of free play were observed at 5 months (62 EL infants, 47 infants at typical likelihood (TL)) and 10 months (101 EL siblings, 77 TL siblings). The newly-developed Parent-Infant/Toddler Coding of Interaction (PInTCI) scheme was used, focusing on global characteristics of infant and parent behaviors. Coders were blind to participant information. Linear mixed model analyses showed no significant group differences in infant or parent behaviors at 5 or 10 months of age (all  $p \geq 0.09$ ,  $d \leq 0.36$ ), controlling for infant's sex and age, and parental educational level. However, without adjustments, EL infants showed fewer and less clear initiations at 10 months than TL infants ( $p=0.02$ ,  $d=0.44$ ), but statistical significance was lost after controlling for parental education ( $p=0.09$ ,  $d=0.36$ ), which tended to be lower in the EL group. Consistent with previous literature focusing on parent-infant dyads, our findings suggest that differences between EL and TL dyads may only be subtle during the first year of life. We discuss possible explanations and implications for future developmental studies.

**Key words:** Autism spectrum disorder, parent-child interaction, infants at elevated likelihood, infancy

During the first year of life, the interaction with parents forms a key aspect of an infant's social environment. In the context of emerging autism spectrum disorder (ASD), investigation of early parent-child interactions (PCI) may provide insight into the developmental course of early social and communicative alterations, before ASD symptoms clinically manifest (Wallace & Rogers, 2010). PCI provide a more naturalistic setting in which these alterations can be signaled than during experimental settings in which behaviors are observed during standardized tests where individuals interact with a professional (Wan, Green, & Scott, 2019). It is important to study the bidirectional nature of interactions and dissect the contribution of both the infant and the parent for determining targets for parent-mediated interventions for ASD (Kasari et al., 2014; Rogers et al., 2014; Wetherby et al., 2014a). In addition, early PCI research may also help to determine targets for *pre-emptive* interventions for infants or toddlers at elevated likelihood (i.e. amelioration of subsequent symptoms to redirect developmental trajectories before the full-blown disorder manifests) (Green et al., 2017; Jones, Dawson, Kelly, Estes, & Jane Webb, 2017; Watson et al., 2017). As research into this domain is relatively new, improved knowledge about how perturbations in early PCI arise and how they change over time, may help to further improve these early parent-mediated (pre-emptive) interventions. The aim of the current study was therefore to investigate differences in PCI in the first year by applying an infant-sibling design. Infant-sibling designs are based on the premise that given the heritability of ASD, infants with an older brother or sister with an ASD diagnosis are more likely (henceforth at Elevated Likelihood (EL)) to develop ASD themselves, compared with infants with an older sibling and no family history of ASD (henceforth at Typical Likelihood (TL)). EL infants have around a 18.7% likelihood of receiving a diagnosis of ASD (Ozonoff et al., 2011) compared to a community prevalence of around 1.7% (Baio et al., 2018). Previous longitudinal studies using a EL design mainly showed that ASD-related precursors and/or early symptoms start to emerge toward the end of

the first year (Jones, Gliga, Bedford, Charman, & Johnson, 2014). However, these EL studies have not yet performed a fine-grained observation of PCI across the first 12 months of life and may have missed more subtle alterations.

#### *Differences between EL and TL dyads during the first year*

Previous retrospective and prospective research indicates that the interaction between parents and infants later diagnosed with (or at elevated likelihood of) ASD in the first year of life differs from the interaction between parents and typically developing infants (Campbell, Leezenbaum, Mahoney, Day, & Schmidt, 2015; Choi, Shah, Rowe, Nelson, & Tager-Flusberg, 2019; Harker, Ibanez, Nguyen, Messinger, & Stone, 2016; Northrup & Iverson, 2015; Rozga et al., 2011; Saint-Georges et al., 2011; Steiner, Gengoux, Smith, & Chawarska, 2018; Trevarthen & Daniel, 2005; Wan et al., 2012, 2013; Yirmiya et al., 2006). A few *retrospective* home video studies have focused specifically on differences in parent-infant interaction between infants subsequently diagnosed with ASD and controls (Saint-Georges et al., 2011; Trevarthen & Daniel, 2005). Results revealed that infants who were later diagnosed with ASD (n=15) differed from typically developing infants (n=15) in their levels of social orientation, receptiveness to the parent, and seeking behaviors (i.e. spontaneous and intentional communication) across the first year (Saint-Georges et al., 2011). Their parents tended to use more stimulation while initiating interaction and fewer gestures in response to their child. Although retrospective home video research can provide insight into the developmental course of ASD, it also has its shortcomings, including a bias resulting from what parents make available for study and variability in the content of home videos (e.g. different settings). The key to overcome these issues is to prospectively study the interaction between parents and infants who are at elevated likelihood of developing ASD because they have an older sibling diagnosed with ASD (Szatmari et al., 2016).

To date, only one *prospective* study investigated parent-infant dyads in EL and TL siblings during the first months of life (Yirmiya et al., 2006). A microanalysis of parent and infant affective states at 4 months showed a weaker synchrony in infant-led interactions (i.e. baby leads, parent follows) in EL (n=21) as compared to TL dyads (n=21), suggesting that the parents of EL infants experience difficulties in adapting their affective behaviors to the affect initiated by the infant. With regard to infant behaviors during the second half-year of life, 6 to 10-month old EL siblings (n=45) tended to be less lively than LR siblings (n=47), as shown by lower global ratings of physical activity during play interaction (Wan et al., 2012, 2013). This may suggest an underlying lower initiation or motivation to socialize. In addition, EL siblings later diagnosed with ASD (n=21) and TL siblings (n=34) produced fewer gestures and gesture-speech combinations at 12 months than EL siblings who did not develop ASD (n=34) (Choi et al., 2019). Lower gesture use of TL siblings, compared to that of EL siblings without ASD, was somewhat unexpected, considering previous work that suggests lower gesture use in EL infants than in TL infants (Cassel et al., 2007). Campbell et al. (2015) concluded that EL siblings subsequently diagnosed with ASD (n=10) were less socially engaged when interacting with their parents at 11 months than TL siblings (n=27), as indicated by a lower global rating of infant reciprocity with the parent and lower frequency of giving and showing toys. However, the same study reported similar levels of social engagement based on the frequency of directed vocalizations and shared positive affect. The latter findings were confirmed by other studies, showing no differences in the first year between EL and TL siblings in attentiveness toward a parent (Steiner et al., 2018; Wan et al., 2012, 2013), positive affect (Wan et al., 2012, 2013), directed gaze (Rozga et al., 2011), smiles (Harker et al., 2016; Rozga et al., 2011), gestures (Talbot, Nelson, & Tager-Flusberg, 2015), vocalizations (Northrup & Iverson, 2015; Rozga et al., 2011; Talbot, Nelson, & Tager-Flusberg, 2016), or integration of communicative behaviors (Parlade & Iverson, 2015).

With regard to parental behavior, research has shown that the parents of EL siblings aged 6 to 12 months are more directive when interacting with their infant than the parents of TL siblings of the same age (Harker et al., 2016; Steiner et al., 2018; Wan et al., 2012, 2013), involving a more parent-directed course of the interaction including intrusive or demanding behaviors (e.g. redirecting child's attention). Given that parents of EL siblings may apply their learned interaction style based on the interaction with the older child with ASD, infants at elevated likelihood of ASD may receive different social communicative inputs. Sensitivity tends to be similar among the parents of EL and TL siblings (Campbell et al., 2015; Harker et al., 2016; Schwichtenberg, Kellerman, Young, Miller, & Ozonoff, 2019), with a trend for lower sensitivity among the parents of EL siblings (Wan et al., 2012, 2013). Taken together, at least some differences between EL and TL dyads start to arise in the first year of life, which underlines the importance of studying early PCI. However, the evidence is on a preliminary level, and far from conclusive.

#### *Predictive constructs in parent-infant interaction*

In typical development it is well established that parental sensitivity, verbal stimulation of the child's speech, and reciprocity promote the child's social and cognitive development (Feldman, Bamberger, & Kanat-Maymon, 2013; Page, Wilhelm, Gamble, & Card, 2010). In the context of ASD, the importance of studying PCI have been strengthened by increasing evidence suggesting that early dyadic behaviors of both interaction partners predict subsequent development of children later diagnosed with ASD. When considering infant behaviors during PCI, lower levels of *infant attentiveness* to the parent and higher levels of *negative affect* at 12 months have been shown to be predictive for diagnostic outcome (ASD) at 36 months of age (Wan et al., 2013). *Gesture production* at 12 months predicted subsequent receptive language and ASD outcomes of 18 to 36-month old EL children (Choi et al., 2019).



In addition, a retrospective study showed that communicative acts by the infant, like eye contact, social smiling and the quality of joint attention, predict subsequent social responsiveness from 12 months onward, but not before (Clifford & Dissanayake, 2009).

When considering parental behaviors in PCI literature, *sensitive behaviors* that follow into the infant's focus of attention have been shown to be positively related to joint attention and language development of children with (emergent) ASD (Baker, Messinger, Lyons, & Grantz, 2010; Haebig, McDuffie, & Ellis Weismer, 2013; McDuffie & Yoder, 2010; Perryman et al., 2013; Siller & Sigman, 2002). Baker et al. (2010) suggests that one form of sensitivity, *structuring (i.e. scaffolding)*, may play a particular important role in facilitating language development. In contrast, parental behaviors that tend to *negatively control* the child's focus of attention may be negatively associated to later child development. Parental control (i.e. directiveness) predicted slower growth in parent-directed smiles within PCI from 9 to 18 months, while parental responsiveness predicted higher rates of concurrent parent-directed smiles (Harker et al., 2016). Furthermore, a rich home *language* environment (e.g. frequent use of words by parents) around 9 and 15 months predicted child language skills at 24 months (Swanson et al., 2019). Also, parental *affect* during interaction with their child has been shown to predict later social communicative skills and expressive language (Warreyn et al., in prep). Although parental behaviors did not differ by subsequent child diagnostic outcome, previous research has consistently shown that parents play a pivotal role in facilitating broader child development. In addition, there is evidence for the effectiveness of early parent-mediated interventions on the subsequent social-communicative and language development of children with ASD (Kasari et al., 2014; Wetherby et al., 2014b), highlighting the importance of optimizing early PCI.

*The current study*

Inconsistency of results so far is probably in part due to small sample sizes, differences across studies in age ranges and group comparisons (e.g. EL vs. TL, EL-ASD vs. EL no ASD), and the use of coding schemes that do not distinguish between behaviors that are spontaneously initiated by the infant and those made in a response to parental behaviors. The importance of the latter is supported by the fact that in current ASD research initiating and responding joint attention behaviors are treated as separate skills that need to be measured separately (e.g. in measures like the Early Social Communication Scales (ESCS) | Meindl & Cannella-Malone, 2011; Nystrom, Thorup, Bolte, & Falck-Ytter, 2019). In addition, only one prospective study focused on the earliest months of life and did not report findings on parents and infants separately. As mentioned above, the latter is needed to dissect the contribution of both partners for determining targets for interventions. None of the abovementioned studies investigated parent-infant interaction pathways across the first year of life. Thus, research into parent-child dyads focusing on both parent and infant behaviors at different time points in infancy are desirable to complement previous studies.

The current study aimed to advance this area of research by focusing on infant, parent, and dyadic behaviors during interactions between parents and infants at EL and TL of ASD at 5 and 10 months of age. To this end, the Parent-Infant/Toddler Coding of Interaction (PInTCI) was developed, which rates infant/toddler (including both initiations and responses), parent, and dyadic behaviors. Prior research used either a macro-level coding approach (i.e. global rating of qualitative and quantitative characteristics) or a micro-level coding approach (i.e. detailed observation of frequency, duration, and timing of behaviors). Although both approaches complement each other (Mesman, 2010), qualitative aspects of interactions are better captured by global rating scales (Bontinck, Warreyn, Meirsschaut, & Roeyers, 2018). Therefore, the PInTCI was designed as a global coding scheme, including potential predictors for ASD or general cognitive or language development (i.e. parental sensitivity, negative

control, scaffolding, and affect; infant attentiveness, and affect) and constructs that were found to be important precursors in infant social communication (i.e. initiating behaviors, sharing of affect). We examined 195 parent-infant dyads (113 EL, 82 TL) during free-play as part of an ongoing longitudinal study involving a large international sample. On the basis of previous research, we hypothesized that EL dyads at 10 months would show lower ratings of infant social communicative behaviors, higher levels of parental negative control, and lower dyadic reciprocity. No specific hypotheses were formulated regarding parent-infant dyads at 5 months, as no previous prospective research exists. Owing to the bidirectional nature of PCI, we expected effects to be accumulative across time, showing larger differences between groups at 10 months than at 5 months.

## Methods

### *Participants*

As part of the ongoing EuroSibs Autism Research Network ([www.eurosibs.eu](http://www.eurosibs.eu)<sup>1</sup>), 195 infants (113 EL and 82 TL) were assessed at 5 and/or 10 months of age. Ethical approval was given by local ethics committees in participating countries, and parents gave informed consent. The EL infants had at least one older sibling with a community clinical diagnosis of ASD (hereafter: ‘proband’). The TL siblings had at least one older sibling with typical development and no ASD within first-degree family members (as confirmed through a parent interview regarding family medical history). EL and TL families were recruited via well-baby clinics, child care centers, volunteer databases, and advertisements (e.g. in waiting rooms at well-baby clinics). EL families were also specifically recruited through diagnostic and intervention services for ASD, and via events for parents of children diagnosed with ASD. Exclusion criteria for both EL and TL infants included diagnosis of epilepsy, preterm birth (i.e.  $\geq 36$  weeks, N=1 was born at 35 weeks), and genetic syndromes clearly related to ASD in infant or proband (e.g. fragile X syndrome, tuberous sclerosis).

Videotaped parent-child dyads were collected from sites in different countries – there were 45 participants from Belgium, 58 from the United Kingdom, 47 from the Netherlands, and 45 from Sweden. Of the 195 infants, 62 EL infants (32 male, 51.6%) and 47 TL infants (27 male, 57.4%) attended the 5-month visit, and 101 EL infants (53 male, 52.5%) and 77 TL infants (40 male, 51.9%) the 10-month visit. Complete 5- and 10-month data were available for 50 EL infants (25 male, 50.0%) and 42 TL infants (25 male, 59.5%). The n=287 clips were randomly selected from a total sample of N=423 dyads. Most of the excluded n=136

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<sup>1</sup> Participating sites in the current study: Ghent University (Ghent, Belgium), Birkbeck College (London, UK), Radboud University Medical Centre (Nijmegen, the Netherlands), University Medical Centre Utrecht (Utrecht, the Netherlands), Uppsala University (Uppsala, Sweden).

dyads were valid to code (n=104; 76%). However, these clips were excluded because it was decided a priori to code a fixed number of clips due to limited coding resources. The remaining dyads that were excluded were either not assessed (n=26) or invalid to code (n=6). See Table 1 for detailed sample characteristics.

[Table 1 about here]

### *Procedure*

Free play interactions between parents and infants were videotaped. At both time points, parents were instructed to play as usual on a play mat on the floor, without making any additional demands on their child. Instructions and toy categories (i.e. pretend play materials, construction toys, spinning toy, exploratory toy, book) were identical across sites. To keep the context as similar as possible across time, toy categories were kept constant (see Figure 1) and the same parent was involved in the play sessions at both time points. A play session typically lasted about 10 minutes, of which 5 minutes were coded. The observation of the interaction started at the moment that the researcher had left the room, parent and child started the interaction, and the video cameras sufficiently captured both parent and child. By recording 10 minutes, at least 5 minutes of parent-infant play were available for coding. The majority of previous studies focusing on PCI included 3 to 6 minute coding (Campbell et al., 2015; Harker et al., 2016; Wan et al., 2012), emphasizing the usefulness of brief videotaped dyads as a context for measuring parent, infant and dyadic characteristics.

To ensure the quality of video clips across the involved sites, standard procedures were followed and regular quality checks of video clips from each site were arranged by a data monitoring panel. Six coders (one English, one Swedish, two Belgian, two Dutch) were trained to use the coding scheme reliably before they independently coded clips. Throughout

the coding process the coders regularly scored clips on which the inter-rater reliability (IRR) was calculated. In addition, to prevent drift and to ensure reliable scoring throughout, coders regularly scored booster clips on which they received feedback from the trainers (MP, CB). Booster clip scores were included in the inter-rater reliability (IRR) and core analyses.



**Figure 1.** Toys at the 5- and 10-month time point, including similar categories (i.e. pretend play materials, construction toys, spinning toy, exploratory toy, book)

### *Measures*

*Parent-Infant/Toddler Coding of Interaction (PInTCI).* The PInTCI (Pijl, Bontinck, Oosterling, & Warreyn, 2016) was used to evaluate PCI. This global coding scheme was developed after an extensive literature review on characteristics of PCI that predicted ASD or general cognitive or language development in previous research. In our study we aimed to include all constructs found to predict subsequent child development, *and* which could be used in different age groups across early development (5-36 months). Therefore, scales from

existing micro and macro measures were adapted and combined: Coding Interactive Behavior (Feldman, 1998), coding scheme for the Communication Play Protocol (Adamson & Bakeman, 1999; Adamson, Bakeman, Deckner, & Nelson, 2012), Dyadic Communication Measure for Autism (Aldred, Green, & Adams, 2004), Erickson coding scales (Erickson, Sroufe, & Egeland, 1985), Manchester Assessment of Caregiver-Infant Interaction (Wan et al., 2012, 2013), Maternal Behavior Rating Scale (Mahoney & Perales, 2003; Mahoney, Powell, & Finger, 1986), Siller's and Sigman's coding scheme (Siller & Sigman, 2002), Social Interaction Rating Scale (Ruble, McDuffie, King, & Lorenz, 2008), infant coding scales (Clifford & Dissanayake, 2009), scaffolding scales (Baker, Fenning, Crnic, Baker, & Blacher, 2007; Dieterich, Assel, Swank, Smith, & Landry, 2006; Hoffman, Crnic, & Baker, 2006), and coding maternal response behaviours (Flynn & Masur, 2007; Landry, Smith, & Swank, 2006; Lloyd & Masur, 2014). Before the actual application of the coding scheme, there was a period of extensive pilot work during which two of the developers coded ten video clips of EL and TL infants interacting with their parents, including infants in the age range between 0 and 36 months. Based on these codings the developers iteratively revised and improved the rating scales.

The PInTCI consists of five child constructs (attentiveness – initiations – sharing of affect – positive affect – negative affect), five parent constructs (sensitive responsiveness – negative control – scaffolding – positive affect – negative affect), and one dyadic construct (dyadic reciprocity), rated on a 1-7 scale. A score of 1 consistently reflects maladjusted/negative behavior while a score of 7 reflects more adaptive/optimal behavior. A brief description of the PInTCI scales can be found in the Appendix. Coders were blind for likelihood status (i.e. EL, TL).

Inter-rater reliability was calculated for 24 clips (12 5-month and 12 10-month dyads) to investigate the relative agreement between the coders, with values classified as poor (0.00–

0.40), fair (0.41–0.59), good (0.60–0.75), and excellent ( $>0.75$ ) (Fleiss, 1986). Given the need to determine the IRR across sites and to overcome language barriers, the 24 clips were all dyads where English was the primary language spoken. Clips were therefore selected from the English speaking site involved (Birkbeck College London, UK). The coders from the different sites scored the same clips and intraclass correlation (ICC) was calculated across the group of coders. The IRR clips included both EL and TL dyads at both 5 and 10 months of age, and were included in the core analyses. The non-native English coders were aware that the coding of English clips had reliability or booster goals, but they did not have information about which clips were IRR and which were booster clips. Also, coders were informed that part of the coded sample (including English, Dutch, Swedish and Belgian clips) would be randomly selected for a general check by the trainers, to ensure that the coders carefully coded all clips. Coders were blind for likelihood status (i.e. EL, TL) and did not have access to the IRR scores coded by the other coders. Constructs with ICCs (average measures) below 0.60 were removed from further analyses (McHugh, 2012). ICC values showed excellent inter-rater reliability for all PCI constructs at 10 months: ICCs ranged from 0.68 to 0.95 ( $p < 0.01$ ). At 5 months, reliability ranged from good to excellent: ICCs ranged from 0.67 to 0.92 ( $p < 0.01$ ), except for infant initiations (ICC=0.42,  $p > 0.05$ ) and parental negative affect (ICC=0.31,  $p > 0.05$ ). The fair reliability for infant initiations at 5 months was likely caused by a lack of variation in the codes of the IRR clips (i.e. 1 to 4) (Hallgren, 2012). This limited variation may imply that infants in the first half year of life do not often make initiations, or their initiations may only be subtle. In typically developing infants, clear initiative behaviors start to develop at around 8 to 10 months, with gestures such as pointing and showing or alternating gaze (i.e. joint attention) (Bates & Dick, 2002). Similarly, the poor reliability of parental negative affect was likely caused by a limited range of codes (i.e. 6 to 7) (Hallgren, 2012). Apparently the IRR clips only contained parents who did not show clear negative



affect during the interaction with their child. Given the context in which parent-child dyads were recorded, this may also be the case for the rest of the sample. Cross-check analyses using percentage agreement ( $\pm 1$  point difference), showed 92% agreement for infant initiations and 100% agreement for parental negative affect, supporting the idea that a lack of variation mainly caused the lower ICC values. See Appendix for an overview of ICC values. More information about this measure can be obtained from the first author.

### *Statistical analyses*

Given the fact that the PInTCI is a newly developed instrument, it was not possible to reliably estimate the effect size and to run an a priori power analysis. However, the sample size in this study (N=195) was significantly larger than in previous studies (e.g. Choi et al., 2019; Harker et al., 2016; Wan et al., 2013).

To analyze group differences in the parent-child dyads, linear mixed models were used with likelihood status (EL, TL) as fixed factor, time (5 months, 10 months) as repeated measure, and site (Belgium, the Netherlands, the United Kingdom, Sweden) as a random effect to account for within site correlation. A group by time interaction effect was included to analyze group differences over time. This approach was applied because it allowed modelling the statistical dependency among observations by including site as a random effect and enabled the use of information from participants with missing data at random across time (only one time point available for n=63 EL siblings and n=40 TL siblings). The mixed model includes the complete dataset to estimate the means at 5 and 10 months. The difference in means from 5 to 10 months is calculated based on these estimates at each time point whereas the degrees of freedom for the difference is based on the number of subjects that were seen at both time points. Age was variable at the 5- and 10-month time points (between 4 and 7 months, and between 9 and 12 months, respectively), introducing potential noise in results.

Therefore, infant age was included as a covariate. We also adjusted for parental educational level, as a measure of social economical status, and infant sex. Cognitive functioning was not included as a covariate, because measurement of the cognitive development in infants is likely to include components of neurodevelopmental disorders (such as ASD) that make this measure impossible to disentangle from the disorder itself (Dennis et al., 2009). Including the MSEL as a covariate in our analyses may therefore lead to overcorrection. A correction for multiple comparisons was applied, using the false discovery rate controlling procedure with a q-value of 0.05 (Benjamini & Hochberg, 1995). The dependent variables were not normally distributed, which is a prerequisite for variance analyses. Therefore, on all PInTCI variables a Van der Waerden transformation was applied, which transforms raw scores into z-scores corresponding to the estimated cumulative proportion of the distribution analogous to a particular rank (using Statistical Package for the Social Sciences [SPSS] version 22). Data across both time points together were transformed, otherwise data would be standardized to a mean level of zero at both time points preventing the analyses of a main effect of time (and group by time interaction). Analyses were carried out on the transformed values, but to facilitate interpretation of the findings, raw mean scores are reported in the Results and Appendix. Results were similar for raw and transformed data.

## Results

### *Descriptive statistics and correlations*

Independent samples t-tests and chi-squared tests showed no significant differences between the EL and TL groups in infant's sex, parent's sex, or infant's chronological age at either time point (see Table 1). However, at the 10-month time point infant's non-verbal IQ differed between the EL and TL groups ( $t(176)=2.71, p=0.007, d=0.41$ ), showing that the EL siblings had lower levels of cognitive development than the TL siblings. In addition, an association between parental educational level and likelihood status (i.e. EL, TL) was observed for both the 5-month and 10-month time points ( $\chi^2(2)=20.24, p<0.001; \chi^2(2)=16.79, p<0.001$ , respectively). Specifically, parental educational level tended to be lower in EL families.

Table 2 reports the correlations between the PInTCI scales at the separate time points, and between 5- and 10-month codings. At both time points, the correlation between attentiveness toward the parent and dyadic reciprocity exceeded  $r_s > 0.80$ . This indicates the presence of multicollinearity and therefore the dyadic scale was removed from further analyses. Correlations between scales at the 5- and 10-month time point are reported in the Appendix.

[Table 2 about here]

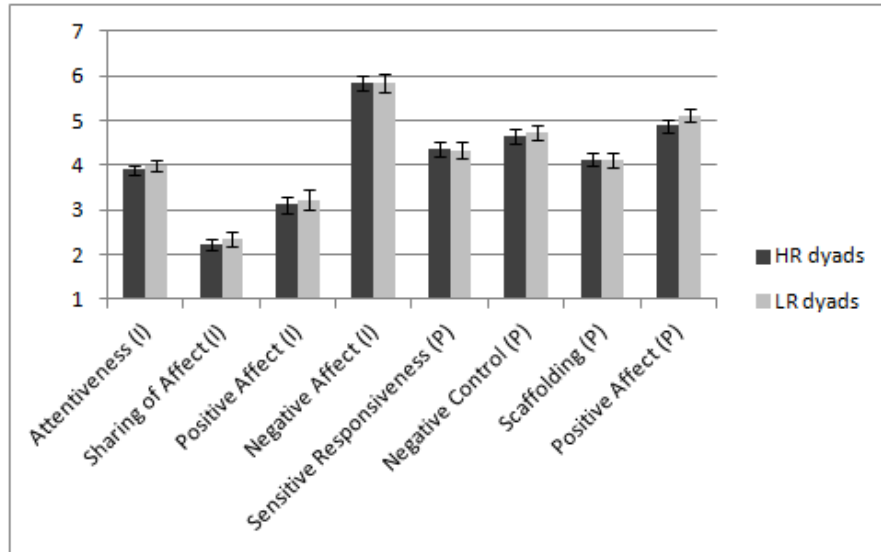
### *Parent-child dyads at 5 and 10 months: group and time effects*

Linear mixed models (LMM) were applied to analyze group differences in the parent-infant dyads (see Table 3 and 4 for details). LMM analysis adjusted for age, sex and parental education revealed no significant main group effects (all  $ps \geq 0.09, d \leq 0.36$ ). However, without adjustments (or solely controlling for infant's age or sex), a significant group effect was found

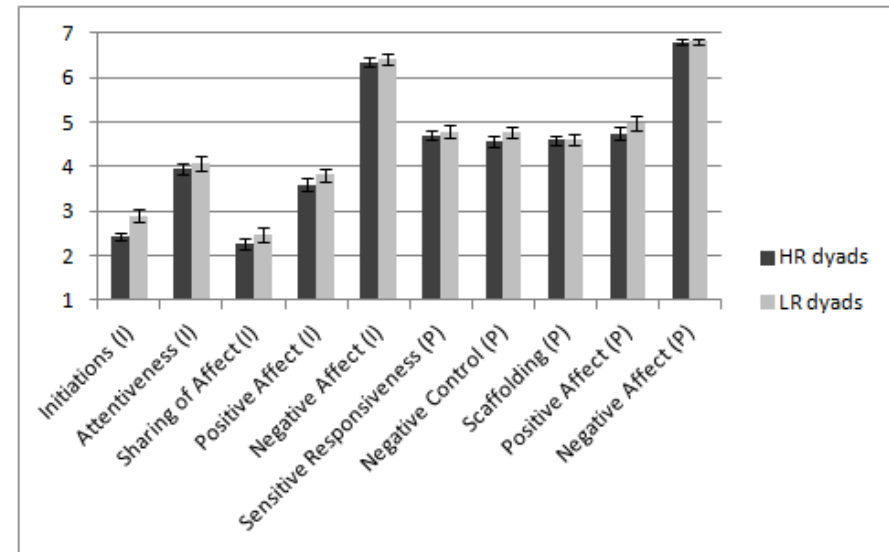
for infant initiations at 10 months ( $F(1, 282.88)=8.57, p=0.02, d=0.44$ ), indicating that EL siblings tend to make fewer and less clear initiations toward their parents than TL siblings. After adjustment for parental education, this effect was only shown as a trend ( $p=0.09, d=0.36$ ), suggesting that the difference was at least partly attributable to different levels of parental education.

Main time effects were found for infant positive affect ( $F(1, 131.20)=16.54, p<0.001, d=0.59$ ), infant negative affect ( $F(1, 140.56)=19.04, p<0.001, d=0.63$ ), parental sensitive responsiveness ( $F(1, 127.38)=9.65, p<0.01, d=0.45$ ), and parental scaffolding ( $F(1, 130.45)=12.20, p<0.01, d=0.51$ ). At 10 months there were higher levels of infant positive affect, parental sensitive responsiveness, and parental scaffolding, and lower levels of infant negative affect than at 5 months. Importantly, no significant group by time interactions were present (all  $ps>0.87$ ), indicating that the changes in parent-infant interactions over time were similar in EL and TL siblings. The random effect of site was not significant (all  $p>0.33$ ), suggesting that the site at which parent-infant dyads were collected did not influence outcomes. See Figure 2 and 3 for the PInTCI ratings at the 5- and 10-month time points by likelihood group and Appendix for detailed information..

[Table 3 and 4 about here]



**Figure 2.** Mean ratings of the Parent-Infant/Toddler Coding of Interaction (PInTCI) at the **5-month** time point by risk group with error bars representing standard errors (1=maladjusted/negative behaviors; 7=more adaptive behaviors).



**Figure 3.** Mean ratings of the Parent-Infant/Toddler Coding of Interaction (PInTCI) at the **10-month** time point by risk group with error bars representing standard errors (1=maladjusted/negative behaviors; 7=more adaptive behaviors).

## Discussion

The purpose of this study was to obtain a detailed picture of the interactions between parents and their 5- and 10-month-old infants at familial EL or TL of ASD. Whereas previous studies investigated PCI mainly starting in the second half of the first year, the current study complements research by prospectively examining PCI at 5 and 10 months through analyses of a large European cohort at elevated likelihood, including both infant's initiating and responding behaviors. Results showed that the newly developed coding scheme had adequate inter-rater reliability for all scales, except for infant initiations and parent negative affect at 5 months (which were removed from further analyses). Our findings revealed no significant group differences after correcting for infant's sex and age, and parental educational level. There were suggestive results that EL infants make fewer and less clear initiations ( $p=0.02$ ,  $d=0.44$ ), but statistical significance was lost once parental education was controlled for ( $p=0.09$ ,  $d=0.36$ ). Examination across time showed higher levels of infant positive affect, parental sensitive responsiveness, and parental scaffolding, and lower levels of infant negative affect at 10 months than at 5 months. These patterns were similar in EL and TL dyads.

The findings support previous research suggesting that behavioral atypicalities in infants who are at elevated likelihood of ASD emerge only toward the end of the first year (Jones et al., 2014). The observed patterns of infant behaviors during PCI (i.e. initiations, attentiveness to parent, shared affect, positive and negative affect) were similar at 5 and 10 months, with EL infants being more likely to show limited social communication than TL infants, but this difference was not statistically significant. This is also in line with previous work focusing on PCI specifically, showing similar levels of social communication abilities during the first year of life, but from the first birthday onward aspects of infant's social

communication (i.e. infant attentiveness, positive affect) predicted later ASD outcome (Wan et al., 2013). However, given that some PCI studies did find significant differences toward the end of the first year (Campbell et al., 2015; Choi et al., 2019), it was to be expected that observable behavioral differences start to emerge at 10 months in our study. Possibly, the lab-based situation may have elicited social desirable behavior in parents, which also influences child behaviors, resulting in non-significant differences between EL and TL dyads. Although the setting was not completely similar to the real-world context, most previous studies have investigated PCI based on a similar setting (i.e. lab-based 3 to 6-minute play). Further, the applied coding scheme may not include all relevant constructs of PCI on which EL and TL dyads tend to differ. However, given that the coding scheme was developed after an extensive literature review on characteristics of PCI that predicted ASD, this is not to be expected. More importantly, the current study did not include information on diagnostic outcomes of infants at elevated likelihood, making it impossible to determine whether the non-significant differences between EL and TL infants were driven by the group of EL infants who were not subsequently diagnosed with ASD.

Without adjustment for parental education, 10-month-old EL siblings tend to make fewer and less clear initiations toward their parents than LR siblings. The direction of this effect is consistent with previous prospective research showing slower growth in the coordination of initiative behaviors of EL siblings who were later diagnosed with ASD as compared to their EL and TL peers (Parlade & Iverson, 2015). However, in the latter study differences were only significant from 12 months onward. Another prospective study found lower levels of liveliness in EL siblings than in TL siblings during the first year (Wan et al., 2012), which may be somewhat related to the trend of lower initiative behaviors found in our study. Across studies, such findings may reflect an initial disruption in social motivation mechanisms, starting with a low drive for social initiative that deprives the child of social

experiences, which, ultimately, leads to more pronounced impairments in social communication (Saint-Georges et al., 2011). This may indicate a prodromal sign in infancy that reflects development of ASD (Yirmiya & Charman, 2010), which may be confirmed by follow-up studies into parent-toddler interactions. However, given the size of the effect in the present study, the difference in initiations between EL and TL infant siblings may not be meaningful. In addition, in the present analysis, the group effect in infant initiations weakened after correcting for parental educational level, suggesting that the group difference was at least partly attributable to different levels of parental education.

One plausible explanation would be that parental educational level affects infant social communicative behaviors. However, it is important to note that we did not find a direct or indirect association between parental educational level and infant social communicative behavior. Although parental educational level was significantly associated with infant non-verbal IQ in our study, we did not find a significant association between infant cognitive functioning and infant initiations for either the EL or TL group (although the association was marginal for the TL group). This implies that there may be other explanations for the reduction of the group effect size for infant initiations at 10 months, instead of a direct impact of parental educational level on parent-child dyads. Two issues may be at stake here. First, in the current study the group of TL parents had higher educational levels than EL parents, which was generally found across all involved sites. Although current findings are inconsistent, previous research suggests that the prevalence of ASD in countries with universal access to diagnostic and intervention services may be higher in lower-SES families than in higher-SES families (e.g. Dodds et al., 2011; Rai et al., 2012), possibly due to a combination of genetic and environmental factors. By entering parental educational level into the models, some of the variance that might actually be about group (i.e. EL, TL) may be taken by parental educational level. Second, the discussion about the role of SES is further



complicated by the fact that there were missing values for parental educational level, reducing the power of the model that included parental educational level. To date, most sibling studies did not enter SES as a variable into their models, which may have influenced outcomes. The current study, together with a few recently conducted studies (Choi et al., 2019; Northrup & Iverson, 2015; Schwichtenberg et al., 2019; Swanson et al., 2019), takes a first step to explore the potential effects of SES, but future studies should further address its role and delineate how to treat this factor in statistical models.

The observed parental behaviors in our study did not differ between EL and TL dyads at 5 or 10 months, implying that EL parents showed similar levels of sensitivity, control, scaffolding and affective behaviors to their infants as compared to TL parents. In line with our results, Campbell et al. (2015) found no differences in macro- and micro-analytically observed parental behaviors between EL and TL dyads. In contrast, other studies found that the parents of EL infants tended to be more directive or demanding than the parents of TL infants (Harker et al., 2016; Steiner et al., 2018; Wan et al., 2012, 2013). Inconsistent findings may be caused by differences between research samples based on specific parental characteristics that affect PCI. These include the presence of the broader autism phenotype (BAP | subclinical characteristics of ASD) or clinical ASD symptoms in parents that may impact on family climate and the way parents interact with their infant (van Steijn, Oerlemans, van Aken, Buitelaar, & Rommelse, 2015). Also, parental stress, which is often elevated in the parents of children diagnosed with ASD, may influence the emotional availability of parents and family adaptive functioning (Estes et al., 2009; Estes, Swain, & MacDuffie, 2019; Hayes & Watson, 2013; Kasari & Sigman, 1997). Further, given that parents of EL siblings might already have received parent-mediated interventions for their child with ASD, learned strategies may have changed their parenting style when they interact with their other children. On the one hand, this may increase differences between EL and TL

families, because TL parents often do not receive any interventions. On the other hand, group differences may be reduced, because interventions tend to support EL parents to remain sensitive and responsive parents, despite the fact that their child may be less responsive. Considering the design of EL infant sibling studies, this may be different in community-based screening studies. A future step will be to include measures focusing on clinical symptomatology, stress, and levels of received parent-mediated intervention to reveal explanatory mechanisms in parent's interactive behaviors.

Independently of group, infant affect, parental sensitivity, and parental scaffolding changed with age. The increased levels of infant positive affect and decreased levels of infant negative affect imply that emotional regulation improves from 5 to 10 months of age, as infants start to use more self-soothing behaviors (e.g., ability to shift attention away from a distressing stimulus) and less crying and fussing as their primary emotion regulation strategies (Calkins & Hill, 2007; Mangelsdorf, Shapiro, & Marzolf, 1995). Furthermore, infants become more interested in playing with objects and this may elicit clearer sensitive and supportive behaviors in the parent. Our findings underline the importance of investigating child and parent behaviors across infancy and raises questions about how these behaviors develop further into toddlerhood. The low correlations between parent-infant interactions at 5 and 10 months, indicating a low stability during infancy, also necessitates more frequent measures of parent-child interaction.

### *Limitations*

Although the current study provides new insights into early PCI using a large prospective sample of EL and TL families, some study limitations should be acknowledged. First, further follow-up of the current sample will allow us to look more closely at patterns of parent-infant interactions in EL siblings with different outcomes (EL with ASD versus EL no ASD). This

provides information about whether differences in social initiations reflect early emerging atypicalities within the BAP or later ASD, and allows the investigation of predictive relationships, which is important given the bidirectional nature of interaction. Although our sample was significantly larger than in previous studies, future work should include even larger samples given the low proportion of familial EL children later diagnosed with ASD (Ozonoff et al., 2011). Second, the multi-site character of this study may have generated more variation in the sample, which may have reduced the power to detect differences. However, a multi-site approach also provides benefits, including a larger sample size and generalizability across countries. Finally, although the PInTCI seems to be a promising measure, our findings should be interpreted with caution given the relatively low percentage of clips on which inter-rater reliability was calculated. However, although the percentage might be different from the common standard, the number of clips ( $n=24$ ) is comparable to previous studies in the field (e.g. Northrup & Iverson, 2015; Talbott et al., 2016; Wan et al., 2012). Furthermore, the IRR clips all contained dyads where English was the primary language spoken, making it impossible to truly randomize across sites. However, the coders did not have information about which English clips were IRR clips and which were booster clips, were blind to likelihood status and did not have access to the IRR scores coded by the other coders. Also, thanks to standard procedures and regular quality checks of video clips at each site, samples were collected in a highly comparable fashion. More research into the PInTCI is required and should include a larger percentage of IRR clips. In addition, the low to medium correlations between the PInTCI scales across time ask for more research into the psychometric properties of the coding measure. Although infant behaviors are likely to vary across the first year due to large developmental changes (i.e. transitioning from a lying, dependent baby to a more independent crawling, babbling (almost) toddler), parent behaviors are expected to be more stable across time. However, given the bidirectional nature of interactions, changes in the

child's development may also explain the lower correlations for parent sensitivity and parent scaffolding. Furthermore, while the coding scheme allowed us to evaluate both qualitative and quantitative aspects of parent-infant interactions while incorporating contextual information, we did not apply a fine-grained micro-coding measure (e.g., Dyadic Communication Measure for Autism (Aldred et al., 2004)). This may be specifically relevant for the construct initiations, given the detailed observation of frequency and timing of behaviors. Also, the additional value of new approaches that efficiently code parent-infant interactions should be investigated, for example by performing musical micro-analysis (Suvini, Apicella, & Muratori, 2017) or automated movement analysis (Lopez Perez et al., 2017).

#### *Conclusions and future recommendations*

In conclusion, this study found no clear differences in parent and infant behaviors between EL and TL dyads during the first year of life. Although it seems plausible that EL siblings (especially those later diagnosed with ASD) exhibit early communicative difficulties, identification of early behavioral markers during the first 12 months is a known challenge for the field. The current analyses present null findings, but a lack of significant differences between groups may not imply equivalent early behaviors. Subtle differences by the end of the first year may be followed by an increasingly atypical development between the first and second birthday (Estes et al., 2015; Landa, Gross, Stuart, & Faherty, 2013). Therefore, longitudinal designs capturing parent-infant and parent-toddler interactions, including subsequent child developmental outcomes, are required. Although our findings ask for additional research into the role of parental education and replication within larger cohorts, they contribute to a growing body of research designed to provide information to support the development of early interventions.

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## Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (13/LO/0751 for BASIS Phase 3 (STAARS); NHS14-1802:1 for EASE; 2011/41, 2014/33, 2015/10 and 2015/81 for Babiétude; and NL42726.091.13 for ZEBRA) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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**Table 1.** Sample characteristics by likelihood group at 5 and 10 months.

	5 months			10 months		
	EL siblings (n=62)	TL siblings (n=47)	$\chi^2 / t$	EL siblings (n=101)	TL siblings (n=77)	$\chi^2 / t$
Sex infant (% male)	51.6	57.4	0.37	52.5	51.9	0.01
Sex parent (% male)	1.6	2.1	0.04	5.0	7.8	0.64
Chronological age (months)	5.3 (0.7)	5.5 (0.6)	1.25	10.3 (0.5)	10.2 (0.5)	-1.26
MSEL Non-verbal IQ <sup>a</sup>	45.1 (6.6)	47.5 (6.7)	1.54	53.7 (7.7)	57.2 (9.5)	2.71*
Educational level parent <sup>b,c</sup> (%)						
<i>Low</i>	40.7	6.8		40.5	12.5	
<i>Medium</i>	37.3	34.1		35.4	33.9	
<i>High</i>	22.0	59.1	20.24**	24.1	53.6	16.79**

\*  $p < 0.05$  \*\*  $p < 0.001$

<sup>a</sup> MSEL non-verbal IQ was based on the visual reception scale and the fine motor scale.

<sup>b</sup> Definition of educational levels: low = primary and/or secondary; medium = tertiary undergraduate; and high = tertiary postgraduate.

<sup>c</sup> Missing values for n=3 EL and n=3 TL siblings at 5 months, and for n=21 EL and n=21 TL siblings at 10 months.

Notes. EL = elevated likelihood; TL = typical likelihood; MSEL = Mullen Scales of Early Learning (Mullen, 1995).

**Table 2.** Spearman correlations between PInTCI scales at the 5- and 10-month time points.

	Infant 1	Infant 2	Infant 3	Infant 4	Infant 5	Parent 1	Parent 2	Parent 3	Parent 4	Parent 5	Dyad
Initiations (Infant 1)		0.52*	0.44*	0.35*	0.07	0.14	0.27*	0.07	0.24	0.12	0.45*
Attentiveness (Infant 2)			0.55*	0.55*	0.12	0.25*	0.22	0.41*	0.40*	0.11	<b>0.86*</b>
Sharing of Affect (Infant 3)		0.54*		0.65*	-0.03	0.16	0.10	0.16	0.38*	-0.04	0.53*
Positive Affect (Infant 4)		0.54*	0.69*		0.13	0.23	0.21	0.22	0.42*	0.05	0.54*
Negative Affect (Infant 5)		0.15	-0.03	0.27		0.03	0.07	0.11	-0.05	0.10	0.07
Sensitive Responsiveness (Parent 1)		0.42*	0.30	0.24	0.20		0.34*	0.56*	0.54*	0.23	0.35*
Negative Control (Parent 2)		0.03	0.14	0.14	0.19	0.17		0.26	0.22	0.18	0.16
Scaffolding (Parent 3)		0.53*	0.27	0.28	0.08	0.67*	0.07		0.41*	-0.01	0.45*
Positive Affect (Parent 4)		0.43*	0.50*	0.56*	0.23	0.41	0.01	0.44*		0.18	0.45*
Negative Affect (Parent 5)											0.17
Dyadic Reciprocity (Dyad)		<b>0.86*</b>	0.49*	0.52*	0.23	0.50*	0.08	0.55*	0.43		

\*  $p < 0.001$ 

Notes. Numbers below diagonal represent 5-month time point, numbers above diagonal represent 10-month time point. **Bold** values indicate correlations  $> 0.80$ . Empty cells indicate that data were removed from core analyses for methodological reasons. PInTCI = Parent-Infant/Toddler Coding of Interaction.

**Table 3.** Summary of the Linear Mixed Model (LMM) analyses focusing on infant behaviors in the PlnTCl, presenting both unadjusted and adjusted models.

			<i>Initiations<sup>a</sup></i>		<i>Attentiveness</i>		<i>Shared Affect</i>		<i>Positive Affect</i>		<i>Negative Affect<sup>b</sup></i>	
			Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>
<i>Unadjusted model (without covariates)</i>	<i>Fixed effect</i>	Group	<b>0.30*</b> (0.10-0.50)	0.44	0.09 (-0.19-0.38)	0.15	0.12 (-0.12-0.36)	0.14	0.15 (-0.09-0.40)	0.15	0.09 (-0.14-0.31)	0.04
		Time	-	-	-0.04 (-0.32-0.23)	0.04	-0.10 (-0.38-0.17)	0.16	<b>-0.43***</b> (-0.71--0.14)	0.59	<b>-0.38***</b> (-0.64--0.12)	0.63
		Time by Group	-	-	0.03 (-0.37-0.43)	0.03	-0.03 (-0.43-0.38)	0.02	-0.05 (-0.48-0.37)	0.04	-0.11 (-0.51-0.28)	0.08
	<i>Random effect</i>	Site	0.04 (0.01-0.28)	-	0.06 (0.01-0.41)	-	0.06 (0.01-0.41)	-	0.06 (0.01-0.44)	-	-	-
<i>Adjusted model (Sex)</i>	<i>Fixed effects</i>	Group	<b>0.30*</b> (0.10-0.51)	0.45	0.09 (-0.19-0.38)	0.15	0.12 (-0.12-0.36)	0.13	0.15 (-0.10-0.40)	0.15	0.09 (-0.14-0.31)	0.05
		Sex	0.09 (-0.11-0.29)	0.13	0.05 (-0.15-0.26)	0.07	-0.14 (-0.34-0.07)	0.19	-0.09 (-0.30-0.13)	0.12	0.15 (-0.04-0.34)	0.23
	<i>Repeated effects</i>	Time	-	-	-0.04 (-0.32-0.23)	0.04	-0.10 (-0.38-0.17)	0.16	<b>-0.42***</b> (-0.71--0.14)	0.59	<b>-0.38***</b> (-0.64--0.12)	0.63
		Time by Group	-	-	0.04 (-0.37-0.44)	0.03	-0.03 (-0.44-0.38)	0.02	-0.06 (-0.49-0.37)	0.04	-0.10 (-0.50-0.29)	0.08
	<i>Random effect</i>	Site	0.04 (0.005-0.28)	-	0.06 (0.01-0.41)	-	0.06 (0.01-0.42)	-	0.06 (0.01-0.44)	-	-	-
<i>Adjusted model (Age)</i>	<i>Fixed effects</i>	Group	<b>0.28*</b> (0.07-0.49)	0.39	0.04 (-0.35-0.44)	0.07	0.08 (-0.29-0.45)	0.06	0.15 (-0.22-0.52)	0.09	0.12 (-0.22-0.45)	0.13
		Age T1	-	-	0.12 (-0.13-0.36)	0.14	0.07 (-0.20-0.34)	0.08	0.25 (-0.02-0.52)	0.27	0.09 (-0.13-0.32)	0.12
		Age T2	-0.04 (-0.25-0.17)	0.06	-0.18 (-0.44-0.08)	0.20	<b>-0.35*</b> (-0.63--0.07)	0.35	<b>-0.41**</b> (-0.70--0.13)	0.42	-0.01 (-0.25-0.24)	0.01
	<i>Repeated effects</i>	Time	-	-	0.03 (-0.30-0.36)	0.06	-0.15 (-0.48-0.18)	0.19	<b>-0.47***</b> (-0.81--0.13)	0.60	<b>-0.46***</b> (-0.78--0.15)	0.57
		Time by Group	-	-	0.04 (-0.45-0.53)	0.02	-0.04 (-0.53-0.46)	0.02	-0.11 (-0.61-0.40)	0.06	-0.01 (-0.48-0.46)	0.01
<i>Random effect</i>	Site	0.03 (0.003-0.26)	-	0.13 (0.01-1.11)	-	0.08 (0.01-0.85)	-	0.04 (0.002-0.67)	-	-	-	

<i>Adjusted model</i>												
<i>(Parental Education)</i>												
<i>Fixed effects</i>	Group	0.30 (0.05-0.54)	0.36	0.10 (-0.22-0.42)	0.10	0.14 (-0.15-0.43)	0.13	0.24 (-0.07-0.54)	0.20	0.03 (-0.25-0.31)	0.02	
	Parental Education		0.14		0.13		0.15		0.07	0.15		
	Low	-0.11 (-0.41-0.20)		-0.19 (-0.49-0.11)		-0.16 (-0.47-0.15)		-0.003 (-0.33-0.33)		-0.04 (-0.33-0.26)		
	Medium	-0.18 (-0.45-0.08)		-0.13 (-0.39-0.14)		-0.20 (-0.48-0.08)		-0.09 (-0.38-0.21)		0.15 (-0.11-0.41)		
	Time	-	-	-0.004 (-0.29-0.28)	0.02	-0.08 (-0.36-0.21)	0.13	<b>-0.42***</b> (-0.72--0.12)	0.57	<b>-0.37***</b> (-0.65--0.09)	0.56	
	Time by Group	-	-	-0.03 (-0.46-0.41)	0.02	-0.04 (-0.48-0.40)	0.03	-0.08 (-0.54-0.38)	0.05	-0.09 (-0.52-0.33)	0.06	
<i>Repeated effects</i>	Site	0.04 (0.004-0.32)	-	0.07 (0.01-0.46)	-	0.08 (0.01-0.55)	-	0.06 (0.01-0.53)	-	-	-	
<i>Random effect</i>												

\*  $p \leq 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

<sup>a</sup> Time and age T1 parameters are not shown given that the 5-month time point was removed from core analyses.

<sup>b</sup> Site parameters were redundant and could not be computed.

Notes. All  $p$ -values were FDR corrected. **Bold** values indicate  $p$ -values  $\leq 0.05$ . Reference levels: Group=EL siblings; Time=10-month time point; Sex=male; Parental education=high.

**Table 4.** Summary of the Linear Mixed Model (LMM) analyses focusing on parent behaviors in the PInTCI, presenting both unadjusted and adjusted models.

			<i>Sensitive Responsiveness</i>		<i>Negative Control</i>		<i>Scaffolding</i>		<i>Positive Affect</i>		<i>Negative Affect<sup>a</sup></i>	
			Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>	Estimate (95% CI)	<i>d</i>
<i>Unadjusted model (without covariates)</i>	<i>Fixed effect</i>	Group	0.09 (-0.17-0.34)	0.07	0.22 (-0.05-0.48)	0.21	0.02 (-0.25-0.29)	0.05	0.15 (-0.10-0.39)	0.21	-0.06 (-0.19-0.06)	0.15
		<i>Repeated effects</i>	Time	<b>-0.30**</b> (-0.58--0.03)	0.45	0.05 (-0.21-0.31)	0.01	<b>-0.38**</b> (-0.64--0.11)	0.51	0.04 (-0.21-0.29)	0.10	-
		Time by Group	-0.07 (-0.47-0.34)	0.05	-0.08 (-0.47-0.30)	0.06	0.03 (-0.36-0.43)	0.03	0.06 (-0.32-0.44)	0.05	-	-
	<i>Random effect</i>	Site	0.12 (0.02-0.71)	-	0.03 (0.002-0.36)	-	0.03 (0.003-0.28)	-	0.11 (0.02-0.68)	-	0.06 (0.01-0.33)	-
<i>Adjusted model (Sex)</i>	<i>Fixed effects</i>	Group	0.09 (-0.17-0.34)	0.07	0.21 (-0.06-0.49)	0.21	0.02 (-0.25-0.29)	0.05	0.15 (-0.10-0.40)	0.21	-0.06 (-0.19-0.06)	0.15
		Sex	-0.04 (-0.25-0.16)	0.06	0.03 (-0.20-0.26)	0.04	0.06 (-0.16-0.28)	0.07	-0.14 (-0.36-0.09)	0.18	0.01 (-0.11-0.14)	0.03
	<i>Repeated effects</i>	Time	<b>-0.30**</b> (-0.57--0.03)	0.45	0.05 (-0.21-0.31)	0.01	<b>-0.38**</b> (-0.64--0.11)	0.51	0.04 (-0.21-0.29)	0.10	-	-
		Time by Group	-0.07 (-0.47-0.34)	0.05	-0.08 (-0.47-0.31)	0.06	0.04 (-0.36-0.43)	0.03	0.06 (-0.32-0.43)	0.04	-	-
	<i>Random effect</i>	Site	0.12 (0.02-0.71)	-	0.03 (0.002-0.36)	-	0.03 (0.003-0.28)	-	0.11 (0.02-0.68)	-	0.06 (0.01-0.33)	-
<i>Adjusted model (Age)</i>	<i>Fixed effects</i>	Group	-0.002 (-0.34-0.34)	0.01	-0.04 (-0.41-0.32)	0.01	-0.10 (-0.49-0.28)	0.05	0.18 (-0.17-0.53)	0.19	-0.08 (-0.21-0.05)	0.19
		Age T1	-0.06 (-0.31-0.18)	0.08	-0.13 (-0.40-0.14)	0.14	0.06 (-0.21-0.33)	0.06	-0.01 (-0.28-0.26)	0.01	-	-
		Age T2	-0.07 (-0.32-0.19)	0.08	-0.04 (-0.33-0.24)	0.04	<b>-0.34*</b> (-0.63--0.05)	0.34	<b>-0.34*</b> (-0.63--0.05)	0.34	-0.003 (-0.13-0.12)	0.01
	<i>Repeated effects</i>	Time	<b>-0.42**</b> (-0.74--0.11)	0.51	-0.06 (-0.35-0.23)	0.01	<b>-0.34*</b> (-0.65--0.02)	0.36	-0.04 (-0.31-0.24)	0.03	-	-
		Time by Group	0.02 (-0.45-0.49)	0.01	0.11 (-0.31-0.54)	0.08	0.10 (-0.37-0.56)	0.06	0.02 (-0.38-0.43)	0.02	-	-
	<i>Random effect</i>	Site	0.09 (0.01-0.88)	-	0.01 (0.00-4.35)	-	0.07 (0.01-0.78)	-	0.17 (0.02-1.49)	-	0.06 (0.01-0.33)	-



<i>Adjusted model (Parental Education)</i>	<i>Fixed effects</i>	Group	0.08 (-0.21-0.36)	0.01	-0.04 (-0.36-0.28)	0.04	0.11 (-0.20-0.42)	0.06	0.28 (-0.01-0.57)	0.25	-0.15 (-0.28--0.02)	0.34
		Parental Education		0.22		0.25		0.10		0.22		0.17
		Low	-0.29 (-0.58--0.001)		-0.36 (-0.70--0.01)		-0.16 (-0.48-0.17)		-0.09 (-0.42-0.24)		-0.12 (-0.29-0.04)	
	Medium	-0.04 (-0.30-0.22)		-0.33 (-0.64--0.02)		-0.03 (-0.32-0.26)		-0.31 (-0.61--0.01)		-0.10 (-0.24-0.05)		
	<i>Repeated effects</i>	Time	<b>-0.27**</b> (-0.56-0.01)	0.47	-0.005 (-0.27-0.26)	0.01	<b>-0.36***</b> (-0.63--0.09)	0.57	0.07 (-0.19-0.33)	0.05	-	-
		Time by Group	-0.17 (-0.60-0.27)	0.11	-0.01 (-0.41-0.40)	0.01	-0.11 (-0.52-0.31)	0.07	-0.07 (-0.46-0.33)	0.05	-	-
	<i>Random effect</i>	Site	0.18 (0.03-1.03)	-	0.03 (0.001-1.09)	-	0.07 (0.01-0.55)	-	0.15 (0.03-0.87)	0.15	0.36 (0.07-1.90)	-

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

<sup>a</sup> Time and age T1 parameters are not shown given that the 5-month time point was removed from core analyses.

Notes. All  $p$ -values were FDR corrected. **Bold** values indicate  $p$ -values  $\leq 0.05$ . Reference levels: Group=EL siblings; Time=10-month time point; Sex=male; Parental education=high.