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Citation for published version:
Dean, B, Ginnell, L, Ledsham, V, Tsanas, A, Telford, E, Sparrow, S, Fletcher-Watson, S & Boardman, JP 2020, 'Eye-tracking for longitudinal assessment of social cognition in children born preterm', *Journal of Child Psychology and Psychiatry*, vol. N/A, pp. 1-11. https://doi.org/10.1111/jcpp.13304

Digital Object Identifier (DOI):
10.1111/jcpp.13304

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Journal of Child Psychology and Psychiatry

The Journal of Child Psychology and Psychiatry

ACAMH The Association for Child and Adolescent Mental Health

Check for updates

Journal of Child Psychology and Psychiatry **:* (2020), pp **–**

doi:10.1111/jcpp.13304

Eye-tracking for longitudinal assessment of social cognition in children born preterm

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Background and objectives: Preterm birth is associated with atypical social cognition in infancy, and cognitive impairment and social difficulties in childhood. Little is known about the stability of social cognition through childhood, and its relationship with neurodevelopment. We used eye-tracking in preterm and term-born infants to investigate social attentional preference in infancy and at 5 years, its relationship with neurodevelopment and the influence of socioeconomic deprivation. **Methods:** A cohort of 81 preterm and 66 term infants with mean (range) gestational age at birth 28^{+5} (23^{+2}–33^{+0}) and 40^{+0} (37^{+0}–42^{+1}) respectively, completed eye-tracking at 7–9 months, with a subset re-assessed at 5 years. Three free-viewing social tasks of increasing stimulus complexity were presented, and a social preference score was derived from looking time to socially informative areas. Socioeconomic data and the Mullen Scales of Early Learning at 5 years were collected. **Results:** Preterm children had lower social preference scores at 7–9 months compared with term-born controls. Term-born children's scores were stable between time points, whereas preterm children showed a significant increase, reaching equivalent scores by 5 years. Low gestational age and socioeconomic deprivation were associated with reduced social preference scores at 7–9 months. At 5 years, preterm infants had lower Early Learning Composite scores than controls, but this was not associated with social attentional preference in infancy or at 5 years. **Conclusions:** Preterm children have reduced social attentional preference at 7–9 months compared with term-born controls, but catch up by 5 years. Infant social cognition is influenced by socioeconomic deprivation and gestational age. Social cognition and neurodevelopment have different trajectories following preterm birth. **Keywords:** Social cognition; development; prematurity; eye gaze.

Introduction

Preterm birth, defined as birth before 37 complete weeks, affects 10.6% of pregnancies worldwide (Chawanpaiboon et al., 2019). Preterm birth is associated with increased likelihood of neurocognitive impairment, autism and social difficulties in childhood (Bhutta, Cleves, Casey, Cradock, & Anand, 2002; Johnson et al., 2009; Johnson & Marlow, 2017). Difficulties with social interaction can cause educational underachievement (Woodward & Fergusson, 2000) and affect social and occupational functioning in adulthood (Woodward & Fergusson, 1999).

One of the challenges to improving long-term outcomes for preterm infants is early identification of those who will have social difficulties because the preschool years are a period of development when interventions may yield most benefit (Boardman & Fletcher-Watson, 2017; Meredith, 2015). Precise and practical measures of cognition in early life coupled with understanding how early measures relate to later outcomes are required to enable this. Socioeconomic deprivation is also known to impact language and interactional abilities in childhood, including for infants born preterm (Arriaga, Fenson, Cronan, & Pethick, 1998; Ene et al., 2019; Hoff & Ribot, 2015; Landry, Denson, & Swank, 1997; Landry, Smith, Miller-Loncar, & Swank, 1997; Pungello, Iruka, Dotterer, Mills-Koonce, & Reznick, 2009).

We used eye-tracking to provide an objective measure of gaze, that is highly resolved in time and space (Boardman & Fletcher-Watson, 2017), and is feasible and valid in preverbal children (Gillespie-Smith et al., 2016). Gaze behaviour controls the intake of visual information, and responses to visual stimuli can be used to make inferences about underlying cognitive processes, such as attention and preference (Fletcher-Watson, Findlay, Leekam, & Benson, 2008; Fletcher-Watson, Leekam, Benson, Frank, & Findlay, 2009; Liversedge & Findlay, 2000). From shortly after birth, infants preferentially direct their vision to social content and later maintain this preference when presented with multiple object arrays (Gliga, Elsabbagh, Andravizou, & Johnson, 2009) or animated scenes (Frank, Vul, & Johnson, 2009).

Early divergence from this trajectory has been observed in children who later receive a diagnosis of autism (Chawarska, Macari, & Shic, 2013; Jones, Carr, & Klin, 2008), leading to the suggestion that reduced fixation on social content (hereafter, reduced social attentional preference) may be an early marker of atypical social cognition (Gogate, 2020; Imafuku, Kawai, Niwa, Shinya, & Myowa,

Conflict of interest statement: No conflicts declared.

2019). Gaze studies in preterm infants have also shown a consistent pattern of reduced social attentional preference and learning, in both visual and auditory contexts (Frie, Padilla, Aden, Lagercrantz, & Bartocci, 2016; Gogate, 2020; Gogate, Maganti, & Perenyi, 2014; Imafuku et al., 2017; Imafuku et al., 2019; Pereira et al., 2017; Telford et al., 2016). However, the stability of these differences over time, and whether they contribute to the ontogeny of neurodevelopmental and/or cognitive impairment, is unknown. Although children born preterm have increased likelihood of an autism diagnosis (Johnson et al., 2009), there is evidence of an overlapping, but aetiologically distinct, preterm behavioural phenotype characterised by attention, anxiety and social difficulties (Arpi & Ferrari, 2013; Johnson & Marlow, 2011; Montagna & Nosarti, 2016).

In the present study, we used eye-tracking to investigate social cognition, operationalised as social attentional preference to visual stimuli. In three tasks that presented stimuli of increasing social complexity, social content focused on the eye region of a face, a human image in an array of nonhuman images and the presence of humans within a naturalistic scene. We tested two hypotheses: first, preterm infants have reduced social attention preference in infancy, and at 5 years, relative to term-born infants; second, social attentional preference is stable between infancy and 5 years, but the pattern of stability differs in children who were born preterm compared with those born at term. In addition, we investigated the impact of gestational age, socioeconomic deprivation and male sex on social attentional preference, and explored whether social attentional preference is associated with neurodevelopmental scores at 5 years.

Methods

Ethical approval

Ethical approvals were granted from the United Kingdom National Research Ethics Service (South East Scotland Research Ethics Committee 01) for all participants recruited from NHS services, and from the University of Edinburgh School of Philosophy, Psychology and Language Sciences Research Ethics Committee for term infants recruited from the community.

Participants

A cohort of preterm infants (gestational age ≤ 33+0 weeks) and healthy term control infants (gestational age ≥ 37+0 weeks) were recruited between February 2013 and August 2015 from the Royal Infirmary of Edinburgh Neonatal Intensive Care Unit and postnatal wards (Boardman et al., 2020), and the community. Exclusion criteria were as follows: major congenital malformation, congenital infection, parenchymal brain injury (defined as cystic periventricular leukomalacia, haemorrhagic parenchymal infarction and post-haemorrhagic ventricular dilatation). Informed written parental consent was obtained. Infants were invited for assessment using eye-tracking in infancy (7–9 months) and at 5 years. Infant eye-tracking data for a subset of participants have been reported previously (Telford et al., 2016). Age corrected for prematurity was used until 2 years, and chronological age thereafter as per convention (Johnson & Marlow, 2006).

One hundred and forty-seven infants (81 preterm, 66 term) completed eye-tracking at a median age of 8 months, and 70 of them (39 preterm, 31 term) were seen again at 5 years. An additional 10 children (6 preterm, 4 term) were seen at 5 years who had not been able to attend in infancy. Table 1 shows the demographic details of participants. Preterm infants had a lower median Scottish Index of Multiple Deprivation 2016 (SIMD) ranking, and there was a modest group difference in age at assessment for time point 2. There were no statistically significant differences between the children seen and not seen at 5 years in gestational age, birthweight, sex, SIMD rank or social preference score in infancy.

Within the preterm group, 15 (19%) had late-onset sepsis, 5 (6%) necrotising enterocolitis and 33 (41%) bronchopulmonary dysplasia. One baby had a grade 3 intraventricular haemorrhage. Two infants received laser therapy for retinopathy of prematurity during the neonatal period. All infants passed visual acuity assessment at time point 1.

Clinical and socioeconomic deprivation measures

Late-onset neonatal sepsis was defined using the Vermont Oxford Network criteria; positive blood and/or cerebrospinal fluid culture after day 3 of life with either pathogenic bacteria or coagulase-negative staphylococcus combined with signs of infection and a decision to treat with ≥5 days of intravenous antibiotics (Vermont Oxford Network, 2019); necrotising enterocolitis was defined as present if Bell's stage 2 or stage 3 (Bell et al., 1978); and bronchopulmonary dysplasia was defined by need for supplemental oxygen at 36 weeks corrected gestational age. Deprivation was reported using the Scottish Index of Multiple Deprivation 2016 (SIMD). This government tool uses multiple measures to assign a level of deprivation to a small geographical area called a data zone, which is then ranked from most (1) to least (6976) deprived, and reported in quintiles (Scottish Government, 2016).

Eye-tracking procedure

At 7–9 months, the infants were seated on their caregiver's lap, whereas at 5 years they sat independently, on a height-adjustable chair, 50–60 cm from a computer monitor on which the stimuli were presented. The monitor had a diagonal length of 58 cm, aspect ratio 16:9 and resolution of 1920 × 1080 pixels. Stimuli were displayed to fill the screen, whilst maintaining their aspect ratio. MATLAB was used with a Tobii© X60 eye-tracker to play the stimuli and record bilateral eye movements, at a rate of 60Hz, to an accuracy of 0.3 degrees. We performed five-point calibration prior to data collection using animated coloured spirals with sound effects (see Appendix S1, Figure S1). Preterm infants were screened using Keeler© acuity cards at time point 1 and excluded if visual acuity was below the estimated norm for age (Speedwell, 2003).

Eye-tracking tasks

We presented three validated social free-viewing tasks of increasing stimulus complexity (Figure 1) at both time points (Gillespie-Smith et al., 2016). Each task contained a set of stimuli, presented interspersed with stimuli from other, nonsocial tasks in the eye-tracking battery. We used attention grabbers (colourful objects, e.g. a flower, on a black background with sound effects) to ensure visual attention to the screen prior to stimulus onset. These were made gaze-contingent for time point 2 (see Appendix S1, Figure S2).

Table 1 Demographic characteristics of participants

Characteristic	Time point 1			Time point 2		
	Preterm (n = 81)	Term (n = 66)	p-Value	Preterm (n = 45)	Term (n = 35)	p-Value
Mean (range) gestational age at birth/ weeks	28^{+5} (23^{+2}–33^{+0})	40^{+0} (37^{+0}–42^{+1})	**<.001**	28^{+6} (23^{+2}–33^{+0})	40^{+1} (37^{+0}–42^{+0})	**<.005**
Mean (*SD*) birthweight/ grams	1112 (250)	3533 (473)	**<.001**	1085 (257)	3586 (388)	**<.005**
Median (IQR) age testing time point 1/ months[a]	7.9 (6.8–8.7)	8.0 (7.4–9.1)	.349	7.4 (6.6–9.1)	8.0 (7.3–9.3)	.309
Median (IQR) age testing time point 2/ months	n/a	n/a		60.3 (59.9–60.9)	63.3 (60.0–66.4)	**.007**
Sex (M:F)	40:41	37:27	.321	24:21	17:18	.822
Median (IQR) SIMD rank	3576 (1982–5365)	5597 (4610–6537)	**<.001**	3553 (2027–5652)	5578 (4820–6509)	**.003**
% SIMD quintiles	**1: 15%** **2–4: 61%** **5: 24%**	**1: 2%** **2–4: 48%** **5: 50%**		**1: 11%** **2–4: 61%** **5: 27%**	**1: 0%** **2–4: 53%** **5: 47%**	

Normally distributed data reported as mean (standard deviation), and non-normally distributed data reported as median (interquartile range). IQR, interquartile range; SD, standard deviation; SIMD, Scottish Index of Multiple Deprivation 2016. The bold values are significant p-values.
[a]Values for preterm group corrected for gestational age at birth. Student's t-test was used for group comparison of gestational age and birthweight, Mann–Whitney U-test for comparing age at testing and SIMD, and chi-square for sex difference.

Face task. The stimuli were photographs of adult faces (three male, three female) gazing directly ahead with a neutral expression. Each stimulus was displayed for 10 s.

Pop-out task. The eight stimuli comprised a grid-like array of five items: a photograph of a face, a 'face-noise' image and three photographs of non-social items; and a mobile phone, car and bird (Gliga et al., 2009). The 'face-noise' image was an artificial scramble of the pixels in the face photograph to produce a control image with the same dimensions and low-level visual properties, whilst being unrecognisable as a face. Each stimulus was displayed for 10 s.

Social preferential looking task. The stimuli were 12 pairs of photographs of real-world scenes. Each pair contained a social scene (depicting 1 or 2 children) and a control, non-social scene (the same scene with no people). The scenes were shuffled, so each social scene was paired with a different non-

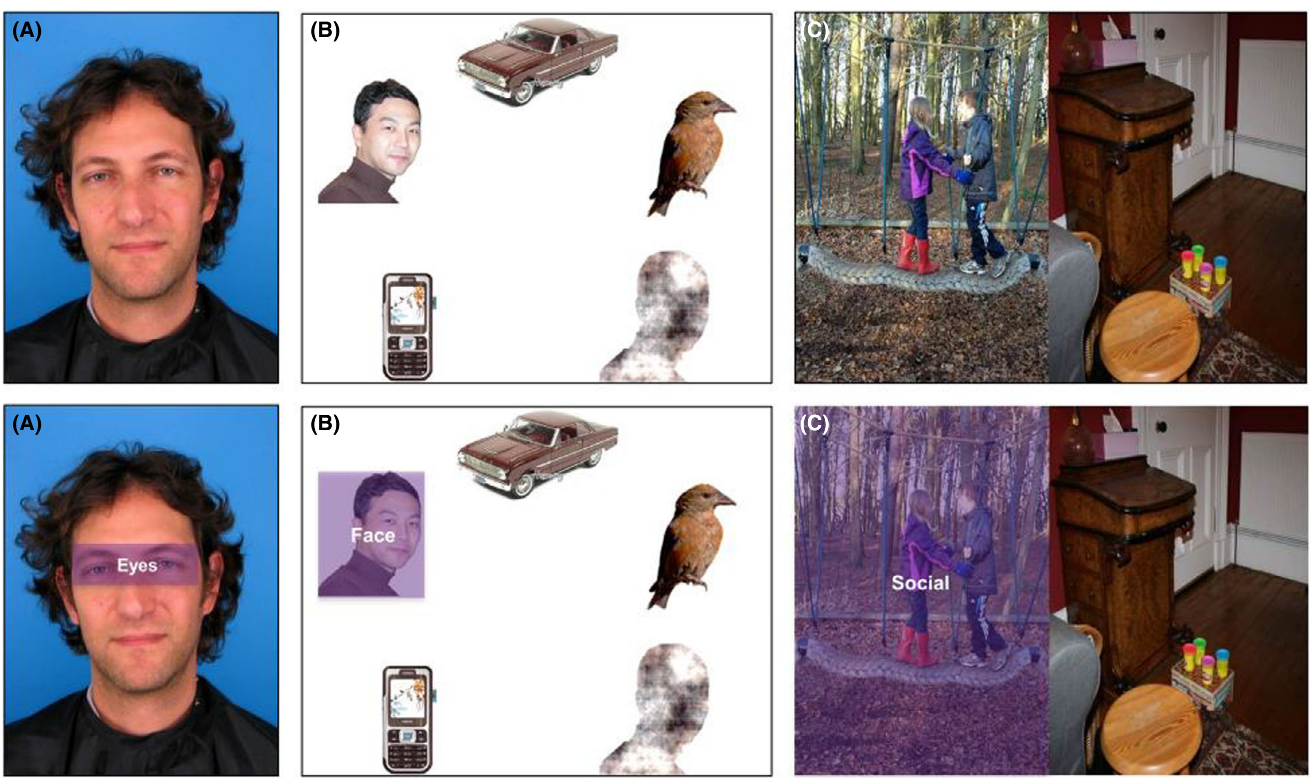

Figure 1 Examples of stimuli for each task with social areas of interest (AOI): (A) Face scanning; (B) pop-out; and (C) social preferential looking

social scene. Each stimulus was displayed for 5 s. For further explanation of the reasons behind shuffling, the scenes and examples of social and non-social versions of the same scene are detailed in the supplemental material (Appendix S1, Figure S2) (Fletcher-Watson et al., 2008; Fletcher-Watson et al., 2009; Telford et al., 2016).

Developmental assessment

All children were assessed at the 5-year appointment using the MSEL (Mullen, 1995), which is an assessment battery designed to measure development from birth to 68 months using a standardised set of age-appropriate objects and stimuli. In this age group, the MSEL assesses developmental attainment over four cognitive domains: visual reception, fine motor, receptive language and expressive language. The Early Learning Composite provides a measure of general cognitive performance and is derived from standardised *t*-scores from the four cognitive domains.

Statistical analyses

We used SPSS version 22 (SPSS Inc, 2013) for statistical analyses, with *p*-values $p < .05$ denoting statistically significant findings. We compared demographic variables (gestational age, birthweight, sex, age at testing, SIMD) using independent-sample *t*-tests, Mann–Whitney *U-test* or chi-square test as appropriate for normally distributed, rank or multinomial data, respectively. Areas of interest (AOI) were predetermined for each eye-tracking task. Raw eye movement data were filtered into fixations using the Tobii© I-VT classification algorithm (Olsen, 2012). Looking time to AOIs and the whole scene were calculated by summing recorded fixation durations over the course of the stimulus display. We excluded trials with a total duration of analysable samples <500 ms. This follows previous convention (Gillespie-Smith et al., 2016; Telford et al., 2016), that is in turn based on the fact that mean fixation duration, regardless of task or context, is 300 ms, whilst mean saccade duration is 80 ms (Liversedge & Findlay, 2000). Thus, we estimated that a total fixation duration of less than 500 ms includes inadequate data to represent a meaningful distribution of fixations to AOIs.

For each task, we predetermined a socially informative AOI as displayed in Figure 1: the eye region in the face task, the face in the pop-out task and the entire social image in the social preferential looking task. We calculated a proportional looking score to the social AOI, across all stimuli within that task, as the ratio of the mean looking time to social AOIs, to the mean looking time to the whole scene:

$$\text{Proportional looking score} = \frac{\text{mean looking time to social AOIs}}{\text{mean looking time to whole scene}}$$

For each individual, an overall social preference score was calculated from the average of the proportional looking scores

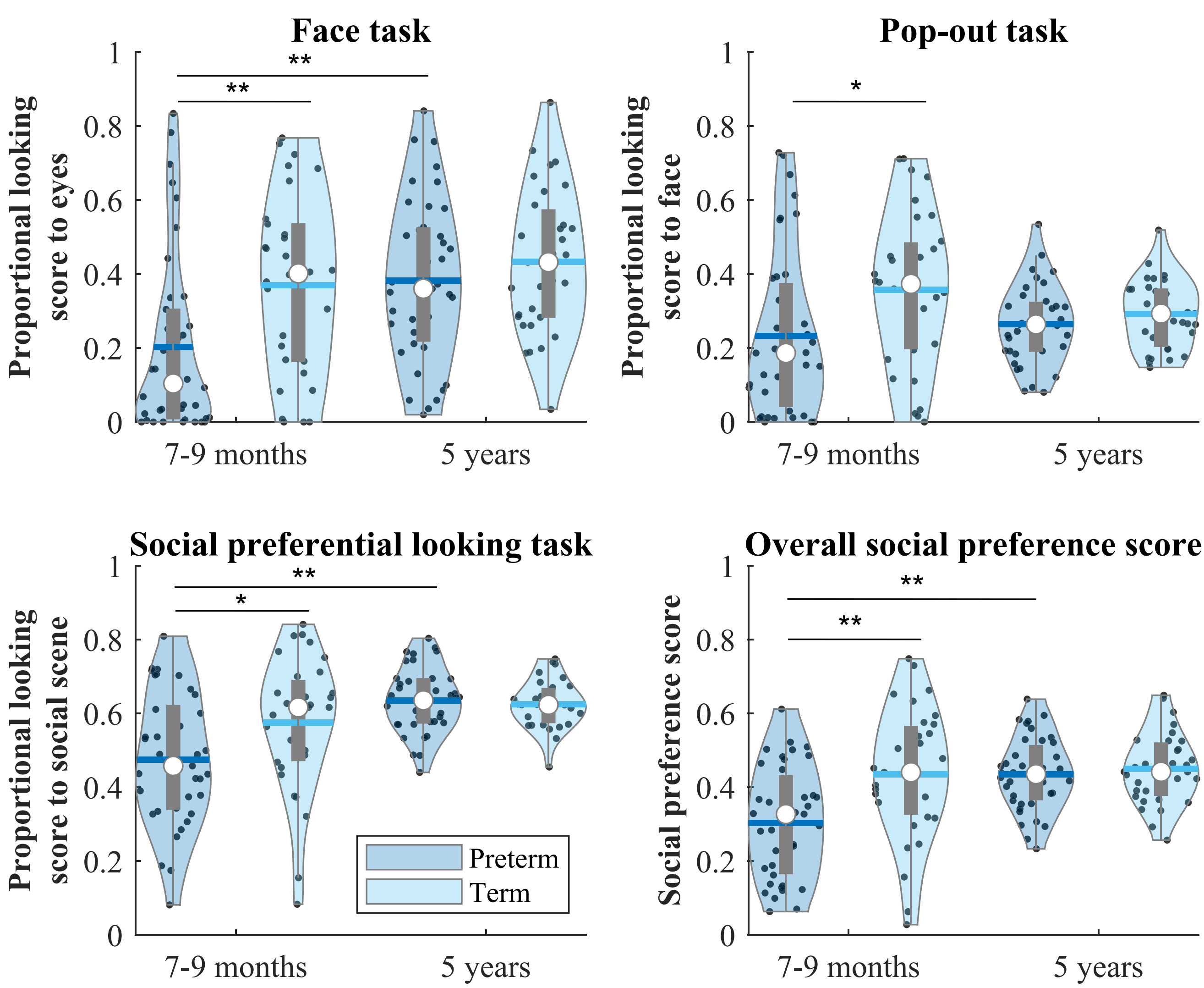

Figure 2 Violin plots of proportional looking score per task and overall social preference score for children with data at both time points (39 preterm, 31 term). *Note:* Created in MATLAB (2018)

Table 2 Eye-tracking data

Task	Measure	AOI	Time point 1 Preterm (n = 81)	Time point 1 Term (n = 66)	Time point 1 p-Value	Time point 2 Preterm (n = 45)	Time point 2 Term (n = 35)	Time point 2 p-Value
Face	Looking time/ ms	Eyes	741 (80–1991)	1228 (387–2613)	.085	1984 (1466–3139)	2764 (1590–3844)	.061
		Mouth	78 (0–496)	75 (0–277)	.569	389 (183–907)	711 (440–1114)	**.019**
		Whole Scene	5125 (3871–6268)	4995 (3738–6187)	.957	5990 (4297–6733)	7000 (6375–7756)	**<.001**
		Eyes-mouth	257 (0–1944)	850 (120–2398)	**.037**	1460 (532–2811)	1679 (561–3265)	.577
	Proportional looking score	Eyes	0.19 (0.01–0.41)	0.28 (0.07–0.50)	.076	0.39 (0.21)	0.42 (0.19)	.559
Pop-out	Looking time/ ms	Face	801 (200–1404)	1268 (410–2485)	**.025**	1558 (1182–2324)	1994 (1456–2459)	.067
		Bird	137 (11–271)	230 (50–367)	**.034**	564 (441–792)	678 (598–955)	**.012**
		Car	277 (144–616)	238 (81–486)	.400	1068 (608–1492)	997 (674–1313)	.996
		Phone	82 (0–168)	104 (50–213)	.069	702 (592–1175)	1068 (755–1399)	**.043**
		Face-noise	144 (73–368)	264 (74–478)	.141	859 (507–1113)	973 (732–1246)	.069
		Whole Scene	4355 (3180–5412)	5419 (4119–6424)	**.002**	6647 (5313–7636)	7004 (6105–7560)	.085
	Proportional looking score	Face	0.19 (0.06–0.32)	0.32 (0.10–0.45)	.062	0.26 (0.10)	0.29 (0.09)	.210
Social preferential looking	Looking time/ ms	Social scene	1222 (716–1578)	1322 (935–1950)	**.049**	2254 (1908–2513)	2370 (2200–2626)	.117
		Non-social scene	666 (481–980)	728 (500–1052)	.543	1291 (917–1689)	1396 (1151–1574)	.636
		Whole Scene	2425 (1930–2872)	2720 (2067–3232)	**.044**	3665 (3234–4110)	3880 (3607–3964)	.079
	Proportional Looking Score	Social scene	0.49 (0.35–0.60)	0.56 (0.45–0.66)	**.025**	0.63 (0.09)	0.63 (0.06)	.962
Overall	Social preference score		0.32 (0.16)	0.39 (0.19)	**.022**	0.42 (0.09)	0.44 (0.09)	.374

Normally distributed data reported as mean (standard deviation), and non-normally distributed data reported as median (interquartile range). The bold values are significant p-values.

for each task (Gillespie-Smith et al., 2016). To avoid skewing means due to missing data, we calculated proportional looking scores if a third of trials were valid, and an overall social preference score was calculated if proportional looking scores were available for all three tasks.

We assessed normality of variable distribution using the Shapiro–Wilk test of normality ($p > .05$) and visual inspection of histograms and Q-Q plots. For normally distributed data, we report mean and standard deviation, and used the independent-sample t-test for between-group comparisons and paired-sample t-test for within-group comparisons. Where data did not meet the normality assumption, we report median and interquartile range, and used the Mann–Whitney U-test and Wilcoxon signed-rank test for between-group and within-group analyses, respectively. Two-way mixed ANOVAs were used to test for interaction of gestational group (preterm, term) and age at appointment (time point 1, time point 2). Partial correlation coefficients were used to account for variable interaction towards determining the statistical strength and statistical significance of relationships. We considered a relationship to be statistically strong if the magnitude of the partial correlation coefficient was above 0.3 (Hemphill, 2003; Tsanas, Little, & McSharry, 2013). Specifically, we computed partial correlation coefficients for the four scores (3 proportional looking scores and overall social preference score) between the baseline attention scores (7–9 months) and the difference in scores between baseline and 5 years, after controlling for age at 7–9 months, age at 5 years, and gestational group (preterm vs. term). The within-subjects factor was implicitly taken into account by using the difference in scores between the baseline and 5-year assessment.

For all participants, we tested associations between social preference score at 7–9 months and 5 years, and the following clinical and demographic variables, using either Pearson's or Spearman's correlation for continuous and discrete variables, respectively, and independent t-tests for dichotomous variables: gestational age, sex and SIMD rank. A hierarchical regression model was used to determine whether variance in social preference score was explained by variables that were significant in correlation analysis. We used Pearson's or Spearman's correlation to test for associations between social preference score, domain t-scores and Early Learning Composite score of the MSEL at 5 years.

Results

Eye movement metrics

The proportion of trials excluded due to looking time <500 ms was 5.9% for preterm and 6.0% for term infants in infancy, and 1.9% for preterm and 0.3% for term-born children at 5 years. Proportional looking scores were available for 98% of the tasks at both time points and social preference score for 95% of preterm and 97% term infants at 7–9 months and 91% and 100%, respectively, at 5 years.

Group-wise analysis of social attentional preference at ages 7–9 months and 5 years

At 7–9 months, preterm infants spent less time looking at socially informative AOIs in all three tasks compared with term-born controls. This was not explained by differences in overall looking time to the whole scene; proportional looking score for the social preferential looking task ($U = 1984$, $z = -2.23$, $p = .025$), and the overall social preference score

Table 3 Partial correlation coefficients for the four scores (3 proportional looking scores and social preference score) between time point 1 (7–9 months) and time point 2 (5 years), controlling for age at 7–9 months, age at 5 years and gestation group

	Within-subject difference for each of the scores			
	Proportional looking score to eyes	Proportional looking score to face	Proportional looking score to social scene	Social preference score
Scores at baseline (7–9 months)				
Proportional looking score to eyes	−0.72	−0.39	−0.43	−0.70
Proportional looking score to face	−0.46	−0.92	−0.44	−0.81
Proportional looking score to social scene	−0.27	−0.50	−0.93	−0.67
Social preference score	−0.66	−0.78	−0.68	−0.90

All statistical relationships were statistically significant ($p < .05$).

(0.32 vs. 0.39, $p = .022$), was lower for preterm infants. At 5 years, the preterm children continued to show differing looking patterns to social informative areas, but there were no significant differences between proportional looking scores on any task, or social preference score, compared with that of controls (Table 2). The present data therefore support our first hypothesis of reduced social attentional preference in association with preterm birth at 7–9 months, but not at 5 years.

Eye-tracking: individual trajectories between 7–9 months and 5 years

A subset of children (39 preterm and 31 term) had eye-tracking at both time points. Infants born at term had stable social attentional profiles between 7–9 months and 5 years, evidenced by similar proportional looking scores to social content for each task and similar social preference score (Figure 2). However, children born preterm had significant increases in proportional looking scores for the face ($z = 3.21$, $p = .001$) and social preferential looking tasks (0.47 vs. 0.64, $p < .001$), and an increase in social preference score (0.29 vs. 0.43, $p < .001$) between 7–9 months and 5 years (Figure 2).

Mixed ANOVAs demonstrated statistically significant interactions between group and age at assessment in the social preferential looking task ($F(1,65) = 5.56$, $p = .021$, partial $\eta^2 = 0.08$) and social preference score ($F(1,60) = 6.21$, $p = .015$, partial $\eta^2 = 0.09$), reflecting gains in the preterm group and stability in the term group. There was no statistically significant interaction in the face ($F(1,66) = 3.19$, $p = .079$, partial $\eta^2 = 0.05$) or pop-out tasks ($F(1,64) = 2.33$, $p = .132$, partial $\eta^2 = 0.04$). Table 3 shows that after controlling for age at 7–9 months, age at 5 years and gestational group (preterm vs. term), there are strong and significant correlations between the baseline scores (7–9 months) and the differences in scores observed between 7–9 months and 5 years. Negative values indicate that lower scores at baseline correspond to greater increases in the 5-year scores.

Associations between social preference score, gestational age, socioeconomic deprivation and sex

At 7–9 months, there was a positive correlation between social preference score and both gestational age ($r_s(135) = 0.20$, $p = .018$) and SIMD rank ($r_s(135) = 0.21$, $p = .014$). There were no positive

Table 4 Hierarchical multiple regression predicting overall social preference score in infancy from gestational age, SIMD rank and sex

	Overall social preference score in infancy					
	Model 1		Model 2		Model 3	
Variable	*B*	β	*B*	β	*B*	β
Constant	0.15		0.14		0.14	
Gestational age	0.01*	0.20	0.00	0.12	0.00	0.12
SIMD rank			0.00*	0.20	0.00*	0.20
Sex					0.01	0.02
R^2	0.039		0.074		0.074	
F	5.28*		5.14**		3.41*	
ΔR^2	0.039		0.035		0.000	
ΔF	5.28*		4.85*		0.03	

SIMD, Scottish Index of Multiple Deprivation 2016.
$N = 132$. *$p < .05$, **$p < .01$.

Table 5 Mullen scales of early learning at 5 years

	Preterm (n = 41)	Term (n = 32)	p-Value
Visual reception	46 (10.71)	52 (41–58)	.080
Fine motor	44 (10.22)	48 (8.40)	.081
Receptive language	46 (10.22)	54 (51–60)	**<.001**
Expressive language	48 (11.40)	54 (5.97)	**.017**
Early Learning Composite	93 (16.68)	104 (10.29)	**.003**

Normally distributed data reported as mean (standard deviation), and non-normally distributed data reported as median (interquartile range). The bold values are significant p-values.

correlations at 5 years ($r_s(76) = 0.10$, $p = .406$ and $r_s(72) = -0.03$, $p = .787$ for gestational age and SIMD rank, respectively). There was no effect of sex on social preference score in infancy, but at 5 years females had a modest increase in social preference score compared with males: mean difference 0.05 (*SE* 0.02), $p = .030$. The present data support the hypothesis of reduced social attentional preference in association with lower gestational age and socioeconomic deprivation at 7–9 months, and male sex at 5 years, but not at both time points.

Gestational age, SIMD rank and sex were entered as factors into a hierarchical regression model to determine whether the addition of SIMD rank and/or sex improved the prediction of social preference score at 7–9 months over and above gestational age alone. The full model of gestational age, SIMD rank and sex to predict social preference score at 7–-9 months (Model 3) was statistically significant, $R^2 = 0.074$, $F(3,131) = 3.41$, $p = .020$; adjusted $R^2 = 0.05$. The addition of SIMD rank (Model 2) led to a statistically significant increase in R^2 of 0.035, $F(1,129) = 4.85$, $p = .029$. The addition of sex did not lead to a significant increase in R^2 (Table 4).

Social preference score and neurodevelopment at 5 years

Table 5 shows MSEL scores at 5 years. There was a significant group difference in Early Learning Composite score, with preterm children scoring lower than term children (93 vs. 104, $p = .003$), driven by lower scores in language domains. There were no significant associations between social preference score at either time point and domain t-scores, or Early Learning Composite score of the MSEL at 5 years. Of note, one child in the preterm group had received a diagnosis of autism by the age of 5 years. Their eye-tracking data were within 1.96 standard deviations of the group mean for all tasks and the overall social preference score at both time points and therefore was not excluded from analysis.

Discussion

The present analyses reveal an atypical social attentional profile in infancy in association with preterm birth, but similar performance to infants born at term by 5 years of age. Furthermore, the findings suggest that socioeconomic deprivation contributes additively to low gestational age for predicting low social attention in infancy. To our knowledge, this is the first study to measure social attentional preferences of preterm infants and controls over early childhood using a consistent set of eye-tracking tasks and taking account of socioeconomic deprivation.

The present findings from infancy are consistent with previous reports of associations between preterm birth and impaired social cognition in visual social attention paradigms in the first year of life (Frie et al., 2016; Imafuku et al., 2017; Pereira et al., 2017). However, the present sample at 5 years demonstrated no evidence of group differences in social attention between preterm children and term-born controls. This is unlikely to be explained by recall bias because there were no significant differences in social preference score in infancy in those seen and not seen at 5 years.

In the present study, data from two time points were examined to observe longitudinal trajectory (trends) in early measures of social attention preferences. There was a significant interaction between group and time points on social preference scores suggesting a different developmental trajectory in preterm children. Given that preterm children show a reduced social attentional profile in infancy compared with term-born controls, but a similar profile by 5 years of age, a plausible explanation is that atypical social attentional profiles at 7–9 months are an early sign of cognitive impairment. This is supported by reports that performance in complex cognitive tasks such as facial recognition is impaired in 5-year-old children who were born preterm (Potharst et al., 2013) and that cognitive impairment persists through childhood and adolescence (Kerr-Wilson, Mackay, Smith, & Pell, 2012; Linsell et al., 2018). Alternatively, U-shaped behavioural change has been described in other domains of infant development (Gershkoff-Stowe & Thelen, 2004); the observed pattern in the data could be explained by preterm the group having a U-shaped trajectory in social attention. Additional assessments at <7–9 months in both groups would be required to investigate this possibility.

A second possible explanation is that the impact of socioeconomic deprivation operates differentially across early childhood, with maximal effects on the earliest development of cognition. Social preference score was correlated with socioeconomic deprivation in infancy but not at 5 years, with hierarchical modelling showing that it explained a modest, but significant, proportion of variance in the social attentional profile in infancy. We believe this to be a novel finding as in previous studies of early visual social attention in preterm infants, socioeconomic deprivation was either not reported or not adjusted for (Frie et al., 2016; Imafuku et al., 2017; Pereira et al., 2017; Telford et al., 2016). This explanation is supported by the observation that socioeconomic deprivation is associated with impaired language development, including among children born preterm (Ene et al., 2019), which is, in part, a social cognitive construct (Hart & Risley, 1995, 2003).

At 5 years, despite a lack of group differences in social preference scores, the preterm group still showed lower Early Learning Composite scores on the MSEL, mainly due to language difficulties. A possible explanation for this is that the deficit in children's more complex social abilities such as language, or interactive abilities, is secondary to reduced social attention during a sensitive window of development in infancy. No relationships were found between infant social preference score and Early Learning Composite or language domain scores on the MSEL; therefore, it is possible that other measures of cognitive function and social interaction through childhood, such as language ability, are required to determine the role of atypical infant social cognition in determining later childhood neurocognitive phenotype following preterm birth.

Preterm birth is very closely associated with cognitive impairment, the neuropathological substrate of which includes diffuse white matter injury and dysmaturation of developing networks. The processes underlying injury and dysmaturation are diverse and include death or failed maturation of pre-oligodendrocytes leading to hypomyelination, axonal injury and subsequent impaired cortical and thalamic development, and thalamic, sub-plate and late migrating GABAergic neuronal injury (Volpe, 2019). Advanced magnetic resonance imaging of infants born preterm reveals atypical cortical and subcortical structural development and 'dysconnectivity' of emerging cerebral networks, and some of these MRI features predict later cognitive deficits (Ball et al., 2015; Batalle, Edwards, & O'Muircheartaigh, 2018; Boardman et al., 2010; Kapellou et al., 2006; Pandit et al., 2014; Telford et al., 2017; van den Heuvel et al., 2015). Specifically, emergent social cognition is associated with white matter microstructure (Elison et al., 2013) and the structural and functional network architectures of the developing 'social brain' are shaped by early life experience (Elison et al., 2013), which are altered in neonates, children and adults who were born preterm.

The strengths of the present study include longitudinal assessment of social cognition in preterm infants assessed using eye-tracking to provide an unbiased assessment of social attention, integrated analysis with standardised tests of neurodevelopment and presence of a control group. In addition, it considered the effect of socioeconomic deprivation defined using a multifactorial measure (Braveman et al., 2005). Finally, another factor adding to the strength of the present study includes the potentially low levels of carryover effects due to the long interval between assessments. Potential limitations of the study are that we did not investigate the possible impact of maternal mental health, which is associated with adverse cognitive and socio-emotional outcomes in school-age children (Kingston & Tough, 2014); neither did we include a measure of maternal cognition in analyses, which could be relevant given that childhood cognition is partly heritable (Benyamin et al., 2014). However, the estimated effect sizes of both determinants are modest so a larger sample size would be required to investigate these issues. The present study did not have sufficient power to investigate the impact of specific comorbidities of preterm birth on social cognition, which could be relevant: for example, bronchopulmonary dysplasia is an independent predictor of cognitive impairment (Twilhaar et al., 2018), and socioeconomic determinants of outcome may be increased among children with comorbidities (Benavente-Fernández et al., 2019; Wolke, 2019). The pop-out task was developed for use in infants and although preference for the face is robust across studies, it is possible that 5-year-olds could respond to other objects in the array differently (e.g. regard the phone as social) which could affect performance (Elsabbagh et al., 2013; Gliga et al., 2009; Telford et al., 2016). Finally, given the possible salience of actions over faces at 5.5 months (Bahrick, Gogate, & Ruiz, 2002), in future work it would be relevant to determine whether group differences in social attention observed at 7–9 months are modified by using stimuli that depict dynamic events.

Conclusions

Preterm infants have reduced social attentional preference at 7–9 months compared with term-born controls, but equivalent social attentional preference by 5 years of age. Despite apparent catch-up, preterm infants continue to demonstrate poorer performance in standardised neurocognitive testing at 5 years, driven by language deficits. Socioeconomic deprivation significantly influences cognitive outcomes, in addition to gestational age, with maximal effects in infancy. Our eye-tracking measure of social attentional preference at 7–9 months was not related to 5-year outcomes; further work is required to determine whether and how infant social cognition plays a role in the ontogeny of cognitive impairment, social difficulties and/or autism, which are all more prevalent among the preterm population. The present data suggest that socioeconomic disadvantage should be considered in studies investigating cognitive development of children born preterm.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Eye-tracking procedure.
Figure S1. Example calibration sequence, running from 1–6.
Figure S2. Examples of social (A and C) and non-social (B and D) versions of the two scenes for the social preferential looking task.
Figure S3. Example attention grabbers.

Acknowledgements

The study was funded by Theirworld (http://www.theirworld.org) and was carried out in the MRC Centre for Reproductive Health (MRC G1002033). The authors are grateful for all families who consented to take part in the study. The authors are also grateful for the provision of stimuli from the University of Stirling (http://pics.psych.stir.ac.uk) and the British Autism Study of Infant Siblings Network (http://www.basisnetwork.org). The authors have declared that they have no competing or potential conflicts of interest.

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Key points

- Preterm birth is associated with atypical social cognition in infancy and with social difficulties and cognitive impairment in childhood.
- The stability of an individual infant's social cognition through childhood and its relationship with neurodevelopment are unknown.
- This study demonstrated that preterm infants have reduced social attentional preference at 7–9 months compared with term-born controls, but catch up by 5 years of age.
- Despite this, the preterm infants continued to demonstrate poorer performance in standardised neurocognitive testing at 5 years, driven by language deficits.
- Further work is required to determine whether infant social cognition plays a role in the ontogeny of cognitive impairment and social difficulties.

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Accepted for publication: 24 June 2020