Predicting cognitive development and early symptoms of autism spectrum disorder in preterm children: The value of temperament and sensory processing

Abstract

This study was the first to longitudinally explore the extent to which early temperament and sensory processing were of predictive value for cognitive development and Autism Spectrum Disorder (ASD) symptomatology in a sample of preterm children ($N=50$, 22 girls, mean gestational age 27 weeks). At the corrected ages of 10, 18, and 24 months, sensory processing and temperament were assessed, as were cognitive development and ASD symptoms at 36 months. Better cognitive development was predicted by fewer hospitalisation days at birth and by lower Activity Level at 18 months. Temperamental subscales of Negative Affect showed associations with both parent-reported and observational measures of ASD symptomatology, whereas sensory processing only had predictive value for parent-reported symptoms of ASD. The usefulness of temperament and sensory processing for prediction of ASD symptom severity and cognitive outcomes became clear in the second year of life. The results indicate that this area of research is worth additional investigation in the extreme and very preterm population, to explore in further detail whether these two concepts might be able to provide information about which preterms are more likely to develop ASD or cognitive impairments.

Key words

very preterm infants

autism spectrum disorder

temperament

sensory processing

cognitive development

1. Introduction

Preterm infants (i.e. children born before 37 weeks of gestation) are at risk for a wide range of short- and long-term complications (Behrman & Butler, 2007). For instance, several studies suggest that preterm birth affects the cognitive abilities of the child (e.g. Allotey et al., 2017), with mean cognitive test scores being significantly negatively associated with birth weight and gestational age (Bhutta, Cleves, Casey, Cradock, & Anand, 2002). As such, preterm children born extremely early, before 28 weeks of gestation, and preterms born very early, between 28 and 32 weeks, are most at risk. Next to impaired cognitive capacities, preterm children also have an increased likelihood to develop Autism Spectrum Disorder (ASD). ASD is a neurodevelopmental disorder, which emerges in childhood and is characterised by difficulties in two main areas. First, people with ASD display persistent deficits in social communication and social interaction. Second, they exhibit restricted, repetitive patterns of behaviour, interests, or activities (Diagnostic and Statistical Manual of Mental Disorders, 5th ed; DSM-5; American Psychiatric Association [APA], 2013). In the general European population, ASD has an estimated prevalence of 0.6% to 1.16% (Baird et al., 2006; Fombonne, 2009). Worldwide ASD prevalence is estimated to be 0.62% (Elsabbagh et al., 2012). In contrast, an ASD prevalence rate estimation of 7% was reported in a meta-analysis of 3366 preterm infants with a median gestation of 28 weeks (Agrawal, Rao, Bulsara, & Patole, 2018). The ASD-likelihood seems to decrease with each additional week of gestational age (Kuzniewicz et al., 2014).

Studies show that a reliable ASD-diagnosis can be made from 2-3 years onwards (Charman & Baird, 2002), although some research indicates that stability of diagnosis is already high as of 18 months or even somewhat earlier (Ozonoff et al., 2015; Pierce et al., 2019). However, at this age, a lot of children with ASD are not yet identified. The mean age of community diagnoses in Europe is about 40 months (Salomone, Charman, McConachie, & Warreyn, 2015). As evidence suggests that interventions yield more improvement the younger the child is at the start of the intervention (Rogers et al., 2012), multiple studies have tried to find early markers that may be used for early identification of ASD. Recently, studies on this matter are mostly done in children with at least one older brother or sister with ASD. These siblings have up to 18.7% chance of developing ASD themselves (Ozonoff et al., 2011) and thus are – next to preterm children – another group at elevated likelihood (EL) for developing ASD. Up till now, no reliable markers of ASD have been consistently identified in children during their first year of life in the domain of social interaction (Zwaigenbaum et al., 2015), although

this is the most obvious area of difficulties in ASD. Looking at other potential markers, there are some indications of motor abnormalities in the first year, e.g. concerning general movements (Einspieler et al., 2014) and head lag (Flanagan, Landa, Bhatt, & Bauman, 2012). However, these problems are not very specific. It is therefore opportune to look for early markers of ASD in other domains. Temperament and sensory features might be good candidates, as they play an important role from birth on, and as group differences between children with ASD and typically developing children on these constructs have already been reported (e.g., Baranek, David, Poe, Stone, & Watson, 2006; Macari, Koller, Campbell, & Chawarska, 2017). Research furthermore indicates that both temperament and sensory features show associations with later ASD symptoms in EL-siblings (e.g., Garon et al., 2016; Baranek et al. 2018). An additional asset of temperament and sensory processing is that they have also been mentioned as predictors of cognitive functioning, mainly in studies with typically developing children (e.g. DiLalla et al., 1990). Thus, given the fact that preterm children are at elevated likelihood to develop both ASD and cognitive impairments, temperament and sensory features may be of particular interest in this population.

1.1. Temperament

The study of temperament has known a long history, with different approaches or ‘traditions’ (see Mervielde & De Pauw, 2012). In the current study, temperament was assessed through instruments based on the psychobiological approach of Rothbart (1981). This approach defines temperament as individual differences in reactivity and self-regulation, with reactivity referring to the excitability and responsivity of a person to external and internal stimuli, and self-regulation referring to the modulation of this reactivity (Rothbart & Derryberry, 1981). For each of the instruments based on this model, factor analysis consistently yielded three main factors of childhood temperament traits (Rothbart & Bates, 2006). The first factor alludes to the extent to which a person tends towards high levels of positive affect. This factor is called Surgency, or Extraversion, and is often referred to as an approach system. People scoring high on Surgency show high activity levels, high-intensity pleasure seeking, impulsivity and low levels of shyness. The second factor is Negative Affect (NA) and refers to the overall susceptibility of the child to experience negative emotions. These first two factors combined encompass most aspects of the reactivity processes mentioned in the temperament definition. The last factor on the other hand, Effortful Control (EC), is tied to self-regulation processes. It covers one’s capacity to regulate reactivity using attention. A second approach of temperament that is adopted in

some of the studies described in the literature overview below, is the one by Thomas and Chess (1977). Research by Mervielde and Asendorpf (2000) showed parallels between the Thomas and Chess concept of Activity and Rothbart's Surgency factor, more specifically Activity Level and Positive Anticipation. Adaptability – the ability to modify reactions to stimuli in a desired way – overlaps with Rothbart's concept of 'Effortful Control', whereas the definition of the Persistence scale (also called 'Attention Span') is very similar to the definition of Rothbart's subscale 'Attentional Focusing'. Quality of Mood is tied to the NA factor of Rothbart. Threshold to Response refers to the amount of stimulation that is necessary to evoke responses in the child, and is as such a very similar concept to the subscale Perceptual Sensitivity of Rothbart. The dimensions of Intensity (the energy level of responses) and Rhythmicity (being unpredictable or irregular) are more difficult to link to a concept of Rothbart, but seem to fit in best under the factor of EC.

1.1.1. Temperament and its association with ASD

Literature points out that the temperamental profiles of preterm and full-term children differ. A number of studies delineate preterm children at the corrected ages of 3-9 months as significantly less adaptable than full-term children (Langkamp & Pascoe, 2001). During this period they also seem to be more negative in mood and more intense (Langkamp & Pascoe, 2001), more unpredictable or irregular (Gennaro, Tulman, & Fawcett, 1990) and less persistent (Spungen & Farran, 1986). This lowered persistence continues at 12 (Hughes, Shults, McGrath, & Medoff-Cooper, 2002) and 24 months (Schraeder & Medoff-Cooper, 1983). These findings seem to be contradicted by those of Sajaniemi, Salokorpi, and von Wendt (1998) who found preterms to be significantly less intense, less active, lower in threshold to respond, and more adaptive and positive in mood than controls at the age of 2. As the link between temperamental features of preterm children and ASD has not yet been investigated, studies on this matter in other populations – such as EL-siblings and children with ASD – could inform our hypotheses concerning the association between temperament and ASD in preterms. Garon and colleagues, for example, explored longitudinal connections between temperament and quantitative ASD symptoms in EL-siblings. At 24 months, both low levels of Behavioural Approach – a combination of the subscales Positive Anticipation, Attention Shifting and Activity Level – (Garon et al., 2009) and lower EC – including the scales Soothability, Low Intensity Pleasure, Inhibitory Control, Attention Shifting, Attention Focus, Activity Level and Anger – (Garon et al., 2016) were associated with more ASD symptoms at 36 months. Macari et al. (2017) furthermore found a link between

Perceptual Sensitivity and autism severity in children with ASD. More specifically, higher autism severity at 43 months was associated with higher ADOS (Autism Diagnostic Observation Schedule, Lord et al., 2000) scores at 26 months and with lower change scores from 26 to 43 months for Perceptual Sensitivity.

1.1.2. Temperament and cognitive development

Studies in preterm children have shown cross-sectional relations between lower scores on cognitive tests and temperamental traits, such as less Persistence, less Approach, low Adaptability and low Activity Level (Ross, 1987). Only a few studies conducted longitudinal research on temperament and cognitive development in preterms. Pérez-Pereira et al. (2016) reported that Approach, High and Low Intensity Pleasure, Sadness, Vocal Reactivity and Soothability as measured with the revised version of the Infant Behavior Questionnaire (IBQ-R; Gartstein & Rothbart, 2003) at 10 months significantly contributed to language development at 30 months. Longitudinal research on this matter has also been conducted in the typically developing population. In both a study of DiLalla et al. (1990) and of Lemelin, Tarabulsky, and Provost (2006), Activity Level was related to IQ at 3 years. However, higher Activity Level was linked to higher IQ scores in the first study, but to lower IQ scores in the second one. Lastly, in the study of Slomkowski, Nelson, Dunn, and Plomin (1992), Affect-Extraversion (encompassing Interest in Persons, Cooperativeness, Fearfulness and Happiness) at age 2 contributed significantly to language scores at age 3. Similar longitudinal studies in EL-siblings or children with ASD have not yet been conducted.

1.2. Sensory processing (SP)

SP refers to the way in which incoming sensory stimuli of the seven sensory systems – the vestibular system, proprioception, vision, taste, hearing, touch and the olfactory sense – are managed by the central and peripheral nervous system (Miller & Lane, 2000). The term SP does not only cover reception, modulation, integration, and organisation of the stimuli, it also encompasses the behavioural responses to the sensory input (Miller & Lane, 2000). As of the latest version of the DSM-5 (APA, 2013), hyper- or hyporeactivity for sensory stimuli, or unusual interest in sensory aspects have become part of the diagnostic criteria for ASD. In this study SP was operationalised by the Infant/Toddler Sensory Profile (ITSP; Dunn, 2002), based on the model of Winnie Dunn. This model assumes an interaction between neurological thresholds and behavioural responses. The neurological

threshold indicates how much stimuli are needed for a child to perceive or react to the stimuli. The behavioural response concerns the way in which a child behaves towards its neurological threshold, passively or actively. The combination of these two concepts results in four quadrants: Sensation Seeking (high threshold, active response by arousing stimulation themselves), Low Registration (high threshold, passive response), Sensation Avoiding (low threshold, active response by trying to avoid the stimuli they perceive) and Sensation Sensitivity (low threshold, passive response). Besides quadrants, the ITSP gives additional information on five sections: auditory-, visual-, tactile-, vestibular- and oral SP.

1.2.1. SP and its association with ASD

Research indicates that preterm children show distinctive SP patterns in comparison to term-born children. A review of Bröring, Oostrom, Lafeber, Jansma, and Oosterlaan (2017) included six studies (Adams, Feldman, Huffman, & Loe, 2015; Bart, Shayevits, Gabis, & Morag, 2011; Crozier et al., 2016; Eeles et al., 2013a; Rahkonen et al., 2015; Wickremasinghe et al., 2013) which investigated their preterm sample with the ITSP. Except for the unambiguous presence of Low Registration, no clear pattern of problems emerged. However, none of these studies investigated the simultaneous presence of difficulties with SP and ASD symptoms. One study by Beranova and colleagues (2017) suggests an association between Sensation Seeking and ASD, as the screening accuracy of ASD in preterms increased significantly when combining the Sensation Seeking subscale with an ASD-screener. Again, evidence from other populations might inform our hypotheses concerning the preterm population, as quite some studies have investigated associations between SP and ASD symptoms in EL-siblings and children with autism. When looking at Restricted and Repetitive Behaviour (RRB), studies by Rogers, Hepburn, and Wehner (2003), Wiggins, Robins, Bakeman, and Adamson (2009), and Wolff et al. (2018) are unanimous that there is a significant relationship between SP and RRB. There is less consistency in the findings concerning the social-communicative deficits or Social Affect factor (SA) of ASD. Rogers et al. (2003) and Wiggins et al. (2009) found no correlation between ADOS_SA and the Short Sensory Profile (Dunn, 1999) in three-year-olds with ASD, whereas Watson et al. (2011) did find a correlation between SA and both Hyporesponsiveness and Sensation Seeking in four-year-olds with ASD. Also in the study of Baranek et al. (2018) elevated Sensation Seeking at 20-24 months was related to higher ADOS_SA in EL-siblings of 3-5 years. However, except for the study by Baranek et al. (2018), all of these studies looked at cross-sectional – instead of longitudinal – associations.

1.2.2. SP and cognitive development

The few prospective studies that have been carried out on the association between SP and cognitive development in preterm children do not reach consensus. Rahkonen et al. (2015) found no association in preterms aged 24 months, whereas Chorna, Solomon, Slaughter, Stark, and Maitre (2014) reported an association between poor tactile responsivity at 12 months and worse motor and language scores at 24 months. The same disagreement can be observed in cross-sectional studies, with Case-Smith, Butcher, and Reed (1998), and Wickremasinghe et al. (2013) finding no relationship between the two concepts, while Buffone, Eickmann, and Lima (2016) concluded that the occurrence of cognitive delay was significantly higher in children with poor SP. Lastly, Eeles et al. (2013b) concluded that a stronger Low Registration and Sensation Avoiding pattern, and less frequent auditory, visual, touch, vestibular, and oral SP behaviours on the ITSP were related to delayed cognitive development at age 2. Factors that might be responsible for the discrepant results are the different measures of IQ and SP, and the different ages of the participants. Evidence from EL-siblings does not provide us with more clear conclusions, as to the best of our knowledge only one study exists on this topic (Wolff et al., 2018). In that study, no associations were found between the Mullen Scales of Early Learning (MSEL; Mullen, 1995) at age 2 and the Sensory Experiences Questionnaire (SEQ; Baranek et al., 2006) in EL-siblings who later developed ASD. The abovementioned evidence on temperamental and sensory markers of ASD symptoms and cognitive development is summarised in the first five columns of Table 1. Only variables from studies providing longitudinal data in preschool children were adopted in this Table. Column five displays the effect sizes (R^2) of the studies. As the R^2 always concerns models including more than only the temperamental or sensory processing variable that was adopted in Table 1 (e.g. IQ, sex, ..), additional β - or t-values for each temperamental or sensory processing variable are reported.

1.3. Conceptual overlap between temperament and sensory processing

Evidence that temperament and sensory processing are related concepts is growing (Mammen et al., 2016). Dunn (2001) suggested that SP forms the basis of temperament. She formulated three hypotheses. First, she assumed that Low Registration enables task performance and thus could be related to EC. Second, she posed that Sensation Seeking is associated with Surgency. Lastly, she proposed that Sensation Avoiding and Sensation Sensitivity are linked to Fear and NA. These

hypotheses were confirmed by a study of Nakagawa, Sukigara, Miyachi, and Nakai (2016) in typically developing children. Studies in children with ASD support some, but not all, of Dunn's hypotheses. In the study of Brock et al. (2012) for example, Sensory Seeking was not related to temperament. Chuang, Tseng, Lu, and Shieh (2012) however did find relations between Sensation Seeking and Surgency, between Low Registration and EC, but also between Low Registration and NA. As work by Green, Ben-Sasson, Soto, and Carter (2012) suggests that SP is related to anxiety in young children with ASD, it is possible that associations between SP and NA are not truly driven by temperament, but by emerging psychopathology.

1.4. Current study

In short, next to cross-sectional associations between temperament and SP on the one hand and cognitive development and ASD symptomatology on the other hand, evidence is emerging that temperament and SP might be of predictive value for cognitive development and ASD in children with ASD, EL-siblings, typically developing children, and preterm children. However, particularly in this last population, studies on this matter are scarce and demonstrate a lack of comprehensiveness. Studies moreover yield inconsistent findings due to variability in research designs, methods, and instruments, different techniques of analysis and differences in participant characteristics such as gestational age or age at the time of the study. The current study had three main goals. First, we were interested to explore the predictive value of early temperament and SP for social-communicative symptoms of ASD in a group of preterm children. We hypothesised that the scales of temperament and SP that emerged from studies with other populations (see Table 1, column 1-5) would also be the scales that predicted ASD symptoms and cognitive development in preterm children. However, as most of the findings in previous studies have not been obtained with the same instruments used in this study, to be able to formulate hypotheses, connections had to be made between the predictive scales of previous studies and the scales of the instruments used in this study (see column 6 of Table 1; the number after each instrument – e.g. IBQ-R_10, ITSP_18 or ECBQ_24 – refers to the age of the children at the time of the assessment, i.e. 10, 18 or 24 months). A lot of the studies that are listed in Table 1 though, used some version of the Toddler Behavior Assessment Questionnaire (TBAQ, Goldsmith, 1996) to assess temperament, which was originally designed to follow up children who had previously been assessed with Rothbart's Infant Behaviour Questionnaire, and was further revised by Rothbart and colleagues. As such, there are some parallels between the TBAQ and the temperamental measures used in this

study, making comparisons a bit easier. Concerning temperament and SP predicting parent-reported social-communicative symptoms of ASD, no previous studies on this matter have been performed. Our study was thus explorative on this part, but based on previous research indicating discrepancies between parental report and observational measures of ASD (e.g. Bishop & Norbury, 2002; de Bildt et al., 2004), it was our hypothesis that different variables might predict observed versus parent-reported social-communicative symptoms. Our second goal was to explore the predictive value of early temperament and SP for the ASD-domain of RRB's. Here too, we expected that some of the variables in Table 1, under the header 'ADOS_RRB' would be the variables predicting observed RRB's, and that the variables predicting observed RRB's would not per se be the ones predicting parent-reported RRB's. Lastly, our third goal was to predict cognitive development at age 3 using early temperamental traits and SP. Again, our hypotheses were derived from previous studies on this topic in other populations. Since subscales of Surgency were particularly prominent for this outcome, it was our hypothesis that especially this temperamental factor would predict cognitive development.

Table 1.

Summary of evidence on temperamental and sensory markers of ASD symptoms and cognitive development, including our hypotheses

	Instrument	Population	Source	Effect Size R ²	Hypotheses
ADOS_SA					
Behavioral Approach (at 24 months)	TBAQ-revised	HR-siblings	Garon et al., 2009	0.44 ($\beta = -0.27$)	ECBQ_24 Activity Level (Surgency) + ECBQ_24 Positive Anticipation (Surgency) + ECBQ_24 Attention Shifting (EC)
Effortful Control (at 24 months)	TBAQ-revised	HR-siblings	Garon et al., 2016	NR	ECBQ_24 Effortful Control + ECBQ_24 Soothability (NA) + ECBQ_24 Frustration (NA) + ECBQ_24 Activity Level (Surgency)
Perceptual Sensitivity (at 26-43 months)	TBAQ-supplemental	children with ASD	Macari et al., 2017	0.32 ($\beta = -0.15$) ^a	ECBQ_24 Perceptual Sensitivity (NA)
Sensation Seeking (at 20-24 months)	SPA	HR-siblings	Baranek et al., 2018	unstandardised B = 0.071	ITSP_24 Sensation Seeking
ADOS_RRB					
Behavioral Approach (at 24 months)	TBAQ-revised	HR-siblings	Garon et al., 2009	0.45 ($\beta = -0.15$)	ECBQ_24 Activity Level (Surgency) + ECBQ_24 Positive Anticipation (Surgency) + ECBQ_24 Attention Shifting (EC)
Effortful Control (at 24 months)	TBAQ-revised	HR-siblings	Garon et al., 2016	NR	ECBQ_24 Effortful Control + ECBQ_24 Soothability (NA) + ECBQ_24 Frustration (NA) + ECBQ_24 Activity Level (Surgency)
Perceptual Sensitivity (at 26-43 months)	TBAQ-supplemental	children with ASD	Macari et al., 2017	0.32 ($\beta = -0.15$) ^a	ECBQ_24 Perceptual Sensitivity (NA)
PARENT-REPORTED MEASURES OF SA					
No predictors found in literature					
PARENT-REPORTED MEASURES OF RRB					
No predictors found in literature					
COGNITIVE DEVELOPMENT					
Positive Anticipation (at 10 months)	IBQ-R	preterms	Pérez-Pereira et al., 2015	0.288 ($\beta = .249$) ^b	IBQ-R_10 Positive Anticipation (Surgency)
High Intensity Pleasure (at 10 months)	IBQ-R	preterms	Pérez-Pereira et al., 2015	0.294 ($\beta = .279$) ^c	IBQ-R_10 High Intensity Pleasure (Surgency)
Vocal Reactivity (at 10 months)	IBQ-R	preterms	Pérez-Pereira et al., 2015	0.294 ($\beta = .294$) ^c	IBQ-R_10 Vocal Reactivity (Surgency)
Low Intensity Pleasure (at 10 months)	IBQ-R	preterms	Pérez-Pereira et al., 2015	0.288 ($\beta = -.402$) ^b	IBQ-R_10 Low Intensity Pleasure (EC)
Soothability (at 10 months)	IBQ-R	preterms	Pérez-Pereira et al., 2015	0.288 ($\beta = .180$) ^b	IBQ-R_10 Soothability (EC)
Sadness (at 10 months)	IBQ-R	preterms	Pérez-Pereira et al., 2015	0.288 ($\beta = -.207$) ^b	IBQ-R_10 Sadness (NA)
Activity Level (at 9 months)	IBR	TDP	DiLalla et al., 1990	0.32 ($\beta = .31$)	IBQ-R_10 Activity Level (Surgency)
Activity Level (at 15 and 18 months)	TBAQ	TDP	Lemelin et al., 2006	0.33 ($\beta = -.21$)	ECBQ_18 Activity Level (Surgency)
Affect-Extraversion (at 24 months)	IBR	TDP	Slomkowski et al., 1992	receptive language: 0.18; t = 2.30 expressive language: 0.25; t = 2.02	ECBQ_24 Surgency + ECBQ_24 Fear (NA)
Poor response to tactile stimuli (at 12 months)	TSFI	preterms	Chorna et al., 2014	NR	ITSP_10 Tactile Sensory Processing

ASD Autism Spectrum Disorder; SA Social Affect; RRB Restricted and Repetitive Behaviour; TBAQ Toddler Behavior Assessment Questionnaire; SPA Sensory Processing Assessment; ITSP Infant/Toddler Sensory Profile; SEQ Sensory Experiences Questionnaire; IBR Infant Behavior Record; IBQ-R Infant Behavior Questionnaire-Revised; TSFI Test of Sensory Function in Infants; HR high risk; TDP typically developing population; ECBQ Early Childhood Behavior Questionnaire; EC Effortful Control; NA Negative Affect, NR not reported

^a: The dependent variable of the regression is ADOS-G, as such the same values are reported for ADOS_SA and ADOS_RRB

^{b, c}: In the article of Pérez-Pereira et al. (2015) three regression analyses were performed with six temperamental variables as independent variables, and word production, mean length of the 3 longest utterances (MLU3), and sentence complexity as the three dependent variables. For each of these six temperamental variables, we report only one of three β 's, namely the one with the highest significance. None of the six temperamental variables loaded most significantly on sentence complexity. ^b dependent variable = word production, ^c dependent variable = MLU3

2. Method

2.1. Participants

Participants were recruited among all children born before 30 weeks of gestation in two Belgian hospitals between May 2012 and June 2013 ($N=97$). In Belgium, very preterm children are systematically followed up at fixed age points by specialised clinical centers. The children were recruited during their first visit at the center, approximately four months (corrected age) after discharge from the hospital. 23 out of the 97 families were not included in the final sample because they did not show up at the first visit ($n=6$), because the pediatrician judged that the parents would not be able to participate in the study due to limited cognitive abilities ($n=2$), because they did not master the Dutch language ($n=13$) or because the child was under supervision of the juvenile court ($n=2$). Seven of the remaining 74 families refused, resulting in a participation rate of 91% ($n=67$). These 67 children were then followed up throughout the first three years of their lives, at the corrected ages of 5, 10, 18, and 24 months, and at the calendar age of 36 months. The data reported in this article were collected during the last four research moments, which took place at the University lab. After every visit the parents received a short written report and some questionnaires, which were to be filled in at home and sent back to the University.

Only participants with sufficient valid data were included for analysis. First, children who did not have any outcome data at 36 months, due to drop-out, were excluded ($n=12$). Second, children who had missing data at 10, 18 and 24 months were removed ($n=5$). This selection process resulted in a final sample of 50 children (Table 2). The children who were excluded for analyses were comparable to the included children on gender ratio ($t(65)=-1.477$; $p=.144$; $\eta_p^2=.032$), gestational age ($t(65)=-0.542$; $p=.590$; $\eta_p^2=.004$), birth weight ($t(65)=-0.622$; $p=.536$; $\eta_p^2=.006$), hospitalisation days ($t(55.144)=1.885$; $p=.065$; $\eta_p^2=.019$), and SES ($t(21.862)=1.194$; $p=.245$; $\eta_p^2=.029$).

Table 2.
Sample characteristics of the included preterms ($n=50$)

	<i>n (%)</i>	
Gender ratio (male/female)	28/22 (56/44)	
Number of twins	24 (48)	
BPD	11 (22)	
IRDS	14 (28)	
IVH grade III/IV	5 (10)	
	<i>M (SD)</i>	<i>range</i>
SES	43.13 (11.99)	12-63.50
Birth weight, g	1024.98 (247.25)	605-1548

Gestational age, <i>weeks</i>	27.24 (1.52)	24-29
Hospitalisation days	77.67 (21.34)	42-124
Age mother at birth, <i>years</i>	30.72 (4.31)	23.04-46.08
Corrected age at time 1, <i>months</i>	10.52 (0.42)	9.73-12.00
Corrected age at time 2, <i>months</i>	18.66 (0.42)	18.00-19.60
Corrected age at time 3, <i>months</i>	24.72 (0.46)	23.40-25.50
Age at time 4, <i>months</i>	36.79 (1.21)	35.33-41.07

M mean; *SD* standard deviation; *BPD* Bronchopulmonary dysplasia; *IRDS* Infant Respiratory Distress Syndrome; *IVH* Intraventricular Haemorrhage; *SES* Socioeconomic Status

2.2. Measures

2.2.1. Sensory Processing

The ITSP (Dunn, 2002; Dutch Translation by Rietman, 2007) is designed to assess sensory modulation abilities of children aged 0-36 months. Separate versions exist for children aged 0-6 months and 7-36 months. The last version is the one used in this study. It comprises 48 items, scored on a scale from 1 (almost always) to 5 (almost never). The items can be combined in four quadrant scores: Sensation Sensitivity, Sensation Avoiding, Sensation Seeking and Low Registration. Furthermore, five sections of sensory systems can be calculated, namely auditory-, visual-, tactile-, vestibular- and oral sensory processing. In this study, parents completed the ITSP when the children were 10, 18, and 24 months old (corrected age). The internal consistency of approximately half of the sections and quadrants of the ITSP exceeded 0.60, the alpha threshold recommended by DeVellis (2016), with values between 0.63 (Auditory Sensory Processing at 24 months) and 0.76 (Auditory Sensory Processing at 18 months and Sensation Seeking at 24 months). The sections and quadrants of the ITSP with alpha's below 0.60 were excluded for analysis.

2.2.2. Temperament

The IBQ-R (Gartstein & Rothbart, 2003; Dutch translation by Roest-de Zeeuw & van Doesum) is a well-validated instrument based on the approach of Rothbart. This parent-reported instrument measures temperament of children aged 3-12 months and is comprised of 191 items, receiving a score from 1 (never) to 7 (always). In order to measure temperament longitudinally, a second questionnaire was needed to cover the age span of the children in our sample. The ECBQ (Putnam, Gartstein, & Rothbart, 2006, Dutch translation by De Kruif et al.) is another well-validated temperament measure based on Rothbart's approach, for toddlers of 18-36 months. The instrument consists of 107 items, again scored on a 7-point Likert scale. Parents filled in the IBQ-R at the

corrected age of 10 months and the ECBQ at the corrected ages of 18 and 24 months. The majority of the alpha's of the higher order scales of the IBQ-R and the ECBQ exceeded the 0.60 threshold (DeVellis, 2016), with values ranging from 0.64 (NA at 10 months) to 0.74 (EC at 18 months). Only the internal consistency of Surgency at 18 and 24 months was below the 0.60 threshold, and the same applied to NA at 24 months. These three higher order scales were not included in the regressions, but were instead substituted by their subscales. For this reason the internal consistency of the subscales making up for the higher order scales with alphas below 0.60 was also assessed. Except for four subscales (High Intensity Pleasure and Sociability at 18 months, and Activity Level and Motor Activation at 24 months), all subscales met the 0.60 threshold, with values ranging from 0.62 (Activity Level at 18 months) to 0.89 (Positive Anticipation at 18 months). The four subscales that did not reach the 0.60 threshold were excluded for analysis.

2.2.3. Cognitive development

At 36 months, cognitive development was assessed with the Mullen Scales of Early Learning (MSEL; Mullen, 1995). The MSEL measure cognitive competence and motor development of children aged 0-68 months. Adding up the subscales Visual Reception, Fine Motor and Receptive- and Expressive Language results in an Early Learning Composite (ELC, $M=100$, $SD=15$).

2.2.4. ASD symptomatology

The ADOS-2 (Lord et al., 2012) is a semi-structured, standardised assessment that is designed to elicit behaviour that is directly relevant to the diagnosis of ASD, on the domains of communication, social interaction, play, and restricted and repetitive behaviour. More ASD symptomatology is translated in higher scores. The ADOS-2 consists of five modules, to enable assessment of children and adults with differing developmental and language levels. In this study, either module 1 ($n=14$) or module 2 ($n=36$) was used. The ADOS-2 administrations at 36 months were performed by ADOS-trained psychologists and were all scored by the second author of this article, who achieved research reliability on the ADOS. We report scores for the subscales Social Affect (ADOS-2_SA) and Restricted and Repetitive Behaviours (ADOS-2_RRB). Calibrated Severity Scores (CSS; range 1-10) were used instead of raw scores, as these CSS are relatively independent of participant characteristics, such as age and verbal IQ, and therefore increase the comparability of scores on different ADOS-modules (Gotham, Pickles, & Lord, 2009).

We assessed parent-reported ASD-related behaviours at 36 months with the preschool version of the SRS-2 (Constantino & Gruber, 2012; Dutch translation by Roeyers, Thys, Druart, De Schryver, & Schittekatte, 2011). More ASD-related behaviours are reflected in a higher score on the SRS-2. The questionnaire comprises 65 items and falls apart in five subscales, that is, autistic mannerisms, social awareness, social cognition, social communication, and social motivation. Furthermore the SRS-2 provides two DSM-5 Compatible Subscales: Social Communication and Interaction (SRS-2_SCI) and Restricted and Repetitive Behaviour (SRS-2_RRB). In this study, raw scores of these last two scales are reported. The internal consistency of the SRS-2 proved to be sufficient in our sample, with alpha's of both the RRB scale (0.66) and the SCI scale (0.77) exceeding the 0.60 threshold (DeVellis, 2016).

2.2.5. Socioeconomic Status

We used the Hollingshead Index (Hollingshead, 1975) to assess SES of each participating family. This index provides a score, ranging from 8 to 66, for each member of the family, based on their education (i.e. years of education and degree) and occupation. In two-parent families, SES was calculated as the mean of the scores of the two parents.

2.3. Data analysis

Five multiple linear regression analyses were performed to predict ADOS-2_SA, ADOS-2_RRB, SRS-2_SCI, SRS-2_RRB, and MSEL at 36 months, using the measures of temperament and sensory-related features at 10, 18, and 24 months as dependent variables. In order not to overanalyse our data, for each outcome variable, we selected no more than four subscales of temperament and/or SP as predictors (Harrell, 2001). These subscales were chosen based on a combination of findings in previous studies (see Table 1) and Pearson's r correlation coefficient analysis. Predictors from Table 1 were only included in our models if they showed a significant correlation with the outcome variable. If this was the case for more than four variables, the four with the highest Pearson's r were selected. We only evaluated infant factors – such as gestational age, hospitalisation days and SES – in our models if significant correlations between these infant factors and the outcome measures were apparent. This was only the case for our MSEL model. For the two SRS-2 models, we also considered possible influences on reporting, such as education, age and gender of the reporting parent. No significant correlations between these factors and SRS-2 were noticed. As described in the introduction, there appears to be some conceptual overlap between the SP and temperamental variables examined in

this study. Although only two of our regression models included both temperamental and sensory processing variables – and these were not the ones that were overlapping according to Dunn (see introduction, paragraph 1.3) – Variance Inflation Factors (VIF), indicating collinearity between the variables in our models, were closely considered. VIF values in all five regression models were however substantially beneath the threshold, so no variables were excluded based on this criterion. Our sample was furthermore characterised by almost 50% of twins. As parent ratings of a twin pair are not independent, we reanalysed the data while excluding one member of each twin pair, which did not change our results significantly. We also reran our five regression models with twin status as a predictor. Twin status was not significant in any of the models. As these two reanalyses of our data indicated that twin status did not alter our results significantly, and as our sample size is already limited, we decided to report the results of our sample while including all the twins and without including twin status as a predictor. In 84% of the cases in our sample, it was the mother who completed the parent-reported questionnaires at all four time points, whereas in 2% of the cases this was always the father. In the remaining 14% a combination of father- and mother report took place. Correlations between the parent-reported outcome measure (SRS-2) and the temperament and SP questionnaires at each time point were compared between the children for which the same parent filled out the questionnaires and the children for which this was not the case. The correlations were not systematically stronger when the SRS-2 and the temperament and SP questionnaires were filled out by the same person.

Although children without sufficient valid data were excluded from analyses (see paragraph 2.1), we still had some missing data, ranging from 2% on the SRS-2 to 22.4% on the ITSP at 24 months. Little's Missing Completely At Random Test (Little MCAR test; Little, 1988) confirmed that data were missing at random ($\chi^2(1194)=710.277, p=1.00$). Expectation Maximization (EM) was used to estimate these missing data.

The Statistical Package for the Social Sciences software version 25 (SPSS Inc., Chicago II, USA) was used to analyse the data. The overall significance level was set at 0.05. As the approach for the SRS-2 was exploratory, the predictors were entered in SPSS in a stepwise way. For the predictors of the other dependent variables, the 'enter' method was used. Assumptions of normality, linearity, homoscedasticity and absence of multicollinearity were met for all five regression analyses.

2.4. Ethics

Approval of the local ethical committee was obtained and a written informed consent was signed by one of the parents of each child.

3. Results

3.1. Preliminary analyses

3.1.1. Correlations between the outcome measures

As in this study ASD symptoms were evaluated with an observational measure (ADOS-2) as well as with a parent-reported measure (SRS-2), Pearson's r correlation coefficient analysis was performed to examine possible correlations between both measures. In case of high correlations, including only one of the two measures in our analysis could be sufficient. However, no significant correlations existed between scores on ADOS-2 and SRS-2 (Table 3). Scores on ADOS-2_SA were significantly correlated with scores on ADOS-2_RRB ($r=.341$, $p=.015$). Analogous, a significant correlation was observed between SRS-2_SCI and SRS-2_RRB ($r=.523$, $p<.001$). Scores on the MSEL were only significantly associated with scores on the SRS-2_RRB ($r=-.387$, $p=.006$), not with ADOS-2.

Table 3.
Correlations between ADOS-2, MSEL and SRS-2 ($n=50$)

	ADOS-2_SA	ADOS-2_RRB	SRS-2_SCI	SRS-2_RRB	MSEL
ADOS-2_SA	1.00				
ADOS-2_RRB	.341*	1.00			
SRS-2_SCI	-.151	.063	1.00		
SRS-2_RRB	.019	.105	.523**	1.00	
MSEL	-.038	.056	-.250	-.387**	1.00

ADOS-2 Autism Diagnostic Observation Schedule-2; SRS-2 Social Responsiveness Scale-2; MSEL Mullen Scales of Early Learning; SA Social Affect; SCI Social Communication and Interaction, RRB Restricted and Repetitive Behaviour

* $p<.05$; ** $p<.01$

3.1.2. Diagnostic and developmental outcome at 36 months

The mean scores on ADOS-2, MSEL and SRS-2, reported in Table 4, suggest that our sample as a whole was not characterised by elevated ASD scores, or by delayed cognitive scores. However, there were some children scoring particularly low or high on these measures. Five children (10%) scored below 70 on the MSEL, three children (6%) scored 130 or higher. On the SRS-2, two children (4%) showed a particular high level of social responsiveness, while 17 children (34%) had mild shortcomings in their social responsiveness. One child (2%) showed severe shortcomings on the

SRS-2. Sixteen children (30%) received ADOS total calibrated severity scores corresponding to an ADOS autism or ASD classification (Hus, Gotham, & Lord; 2014) at 36 months. Eventually, six children received an ASD research diagnosis and an additional six children met the criteria of the BAP at 36 months (see Table 4). Concerning the ITSP, the means of all the subscales at 10, 18 and 24 months fell within the range of normal functioning. Across all three time points, on average 22.74% of our sample scored 'presumably' or 'definitely' higher than others (meaning hyperresponsivity on the five SP sections, and more Low Registration/Sensation Seeking/Sensory Sensitivity/Sensory Avoiding), whereas on average 7.29% scored 'presumably' or 'definitely' lower on these scales.

Table 4.
Diagnostic and developmental outcomes at 36 months (n=50)

	<i>M (SD)</i>	<i>range</i>
ADOS-2 <i>total CSS</i>	2.74 (1.82)	1-9
SRS-2 <i>total T score</i>	57.03 (9.68)	36-80
MSEL	99.16 (19.78)	58-139.48
	<i>n (%)</i>	
diagnosis ASD / with developmental delay	6 (12) / 0 (0)	
BAP / with developmental delay	4 (8) / 2 (4)	
only developmental delay	14 (28)	
none of the above	24 (48)	

M mean; *SD* standard deviation; ADOS-2 Autism Diagnostic Observation Schedule-2; *CSS* Calibrated Severity Score; *SRS-2* Social Responsiveness Scale-2; *MSEL* Mullen Scales of Early Learning; *ASD* Autism Spectrum Disorder; *BAP* Broader Autism Phenotype

3.2. Regression analyses

3.2.1. ADOS-2_SA

A theoretical model containing one sensory and one temperamental subscale, namely ITSP_24 Sensation Seeking ($r=.322$, $p=.023$) and ECBQ_24 Perceptual Sensitivity ($r=.393$, $p=.005$) was put forward to predict ADOS-2_SA. The resulting model was significant ($F(2,47)=5.529$, $p=.007$), with the independent variables accounting for 19% of the variance in ADOS-2_SA scores (Table 5). A significant β was noted for the predictor ECBQ_24 Perceptual Sensitivity ($\beta=.317$, $t=2.244$, $p=.030$).

Table 5.
Regression results for ADOS-2_SA (n=50)

	<i>B</i>	<i>SE B</i>	β	<i>p</i>	<i>R</i> ²	<i>F(df)</i>	<i>p</i>
(constant)	-.827	1.173			.190	5.529 (2,47)	.007
ITSP_24 Sensation Seeking	.043	.030	.205	.153			
ECBQ_24 Perceptual Sensitivity	.505	.225	.317	.030			

ADOS-2 Autism Diagnostic Observation Schedule-2; SA Social Affect; ITSP Infant/Toddler Sensory Profile; ECBQ Early Childhood Behavior Questionnaire

3.2.2. ADOS-2_RRB

Seven predictors emerged out of the literature as possible predictors of ADOS-2_RRB, of which only one – ECBQ_24 Perceptual Sensitivity ($r=.332$, $p=.018$) – showed a significant correlation with this outcome measure in our sample. The overall model (Table 6) was significant ($F(1,48)=5.965$, $p=.018$), accounting for 11.1% of the variance in ADOS-2_RRB, with a significant β for ECBQ_24 Perceptual Sensitivity ($\beta=.332$, $t=2.442$, $p=.018$).

Table 6.
Regression results for ADOS-2_RRB (n=50)

	B	SE B	β	p	R ²	F(df)	p
(constant)	1.784	1.435			.111	5.965 (1,48)	.018
ECBQ_24 Perceptual Sensitivity	.731	.299	.332	.018			

ADOS-2 Autism Diagnostic Observation Schedule-2; RRB Restricted and Repetitive Behaviour; ECBQ Early Childhood Behavior Questionnaire

3.2.3. SRS-2_SCI

As no previous research focused on predicting SRS-2 outcome using temperament and sensory features, it was not possible to compose a model for SRS-2_SCI based on previous findings. Relying on Pearson's r correlation analyses between SRS-2_SCI and all of the temperament and SP scales, the four scales with the highest correlations, i.e. ITSP_24 Low Registration ($r=-.530$, $p<.001$), ECBQ_24 Effortful Control ($r=-.539$, $p<.001$), ECBQ_24 Positive Anticipation ($r=-.550$, $p<.001$), and ECBQ_24 Soothability ($r=-.566$, $p<.001$), were selected as predictors. Eventually, a significant model ($F(2,47)=15.035$, $p<.001$) including ITSP_24 Low Registration ($\beta=-.316$, $t=-2.328$, $p=.024$) and ECBQ_24 Soothability ($\beta=-.394$, $t=-2.900$, $p=.006$) was obtained (Table 7). Together these two independent variables accounted for 39% of the variance in SRS-2_SCI scores.

Table 7.
Regression results for SRS-2_SCI (n=50)

	B	SE B	β	p	R ²	F(df)	p
(constant)	93.645	12.441			.390	15.035 (2,47)	.000
ITSP_24 Low Registration	-.705	.303	-.316	.024			
ECBQ_24 Soothability	-5.060	1.745	-.394	.006			

SRS-2 Social Responsiveness Scale-2; SCI Social Communication and Interaction; ITSP Infant/Toddler Sensory Profile; ECBQ Early Childhood Behavior Questionnaire

3.2.4. SRS-2_RRB

For this outcome measure, the four variables with the highest correlations were ITSP_18 Low Registration ($r=-.446$, $p=.001$), ITSP_18 Auditory Sensory Processing ($r=-.489$, $p<.001$), ITSP_24 Low Registration ($r=-.452$, $p=.001$), and ECBQ_24 Soothability ($r=-.434$, $p=.002$). Stepwise multiple

regression analysis yielded a significant model ($F(2,47)=12.532$, $p<.001$, Table 8), which was able to explain 34.8% of the variance in SRS-2_RRB. This model comprised ITSP_18 Auditory Sensory Processing ($\beta=-.394$, $t=-3.212$, $p=.002$) and ITSP_24 Low Registration ($\beta=-.343$, $t=-2.797$, $p=.007$).

Table 8.
Regression results for SRS-2_RRB (n=50)

	B	SE B	β	p	R ²	F(df)	p
(constant)	20.988	3.559			.348	12.532 (2,47)	.000
ITSP_18 Auditory Processing	-.218	.068	-.394	.002			
ITSP_24 Low Registration	-.189	.068	-.343	.007			

SRS-2 Social Responsiveness Scale-2; RRB Restricted and Repetitive Behaviour; ITSP Infant/Toddler Sensory Profile

3.2.5. MSEL

Eleven temperament and SP scales were retrieved from the literature as possible MSEL predictors. The two retained predictors after correlation analyses were ECBQ_18 Activity Level ($r=-.388$, $p=.005$) and ECBQ_24 Sociability ($r=-.367$, $p=.009$). Furthermore, significant correlations between the MSEL and SES ($r=.337$, $p=.017$), hospitalisation days ($r=-.373$, $p=.008$) and gestational age ($r=.292$, $p=.039$) were noticed. However, as gestational age and hospitalisation days were strongly correlated ($r=-.764$, $p<.000$), we did not correct for both hospitalisation days and gestational age in our model, but selected the one showing the strongest correlation with the MSEL, namely hospitalisation days. The regression analysis generated a significant model ($F(4,45)=5.233$, $p=.002$), accounting for 31.7% of the variance (Table 9). A significant β was observed for hospitalisation days ($\beta=-.265$, $t=-2.066$, $p=.045$) and for ECBQ_18 Activity Level ($\beta=-.272$, $t=-2.120$, $p=.040$).

Table 9.
Regression results for the MSEL (n=50)

	B	SE B	β	p	R ²	F(df)	p
(constant)	157.592	26.692			.317	5.233 (4,45)	.002
hospitalisation days	-.237	.115	-.265	.045			
SES	.266	.231	.161	.254			
ECBQ_18 Activity Level	-6.830	3.222	-.272	.040			
ECBQ_24 Sociability	-3.043	2.718	-.160	.269			

MSEL Mullen Scales of Early Learning; SES Socioeconomic Status; ECBQ Early Childhood Behavior Questionnaire

4. Discussion

This study was the first to investigate temperament and SP longitudinally in relation to ASD symptoms and cognitive development in preterms. Regression analyses indicated that, as of the second year of

life, both temperament and SP had some predictive value for later ASD symptom severity and cognitive development.

4.1. Prediction of social-communicative symptoms of ASD

More parent-reported social-communicative problems on the SRS-2 were predicted by a stronger pattern of Low Registration at 24 months. A possible explanation might be that children who register less of their environment, miss attempts to initiate social interaction from others, have fewer learning experiences, and develop less optimal social skills, as was also suggested by Jones, Gliga, Bedford, Charman, and Johnson (2014). Furthermore, considering temperamental predictors, less Soothability at 24 months showed a significant relationship with higher SRS-2_SCI scores. The relationship between Soothability – a scale belonging to the higher-order factor NA – and social-communicative problems may be quite straightforward. Children with low scores on the Soothability scale have difficulties with regulation, which might cause them to focus mainly on their own emotions instead of on social cues. As in the domain of temperament and SP no evidence was yet available on predictors of the SRS-2, we cannot compare our results with earlier findings. Concerning the observational measure of social-communicative ASD symptoms, no associations with SP were noticed. However, more Perceptual Sensitivity at 24 months – another subscale of NA – was a significant temperamental predictor of higher ADOS-2_SA. Previous research on temperamental predictors of ASD in children with ASD (Macari et al., 2017) also mentioned Perceptual Sensitivity. Children with a high score on this scale notice even very quiet sounds, sights, and small changes in the environment. This may distract them from social interactions, leading to more social-communicative problems.

4.2. Prediction of RRB's in ASD

More parent-reported RRB's at 36 months were predicted by more Auditory Sensory Processing at 18 months and by a stronger pattern of Low Registration at 24 months. Children might develop RRB's to cope with auditory stimuli, which they might perceive as invasive. Our finding of an association between RRB's and Low Registration, on the other hand, could mean that those children who close them off from the outside world at 24 months, are also the ones most occupied with their own world and their RRB's at 36 months. Alternatively, this association could be explained by RRB's being a form of self-stimulation at age 3 for those children who registered few stimuli at 24 months. SP did not have any predictive value for observational measures of RRB, as was also the case for the observational

measures of social-communicative symptoms. Only Perceptual Sensitivity at 24 months was positively associated with ADOS-2_RRB, a subscale that previously already proved to be associated with autism severity in the research of Macari et al. (2017) in children with ASD. Children scoring high on Perceptual Sensitivity perceive a lot of stimuli from the environment, e.g. sights and sounds, which possibly causes them to develop RRB's in order to cope with these multiple stimuli. An alternative explanation is based on the fact that atypical sensory processing is – as mentioned in the introduction – part of the diagnostic criteria for ASD, and more specifically of RRB (DSM-5, APA, 2013). Infants with higher levels of RRB at age 3 may already show these patterns earlier in development, as suggested by our finding of higher Perceptual Sensitivity at age 2. This explanation is furthermore supported by the work of Ben-Sasson et al. (2009), who provided evidence of stability in sensory processing among both typically developing children and children with ASD.

4.3. Prediction of cognitive development

Our regression model revealed a longitudinal association between more hospitalisation days at birth and worse cognitive outcome at 36 months. As number of hospitalisation days was strongly associated with gestational age, we can conclude that severity of prematurity at birth is proportional to preschool cognitive scores. This finding is in line with that of Bhutta and colleagues (2002), who came to the same conclusion in school-aged preterms. Temperament proved to have some additional predictive value on top of the association with hospitalisation days, as lower Activity Level at 18 months was predictive for better cognitive outcome in our sample. This same association was found in the study of Lemelin et al. (2006) in typically developing children. It was suggested by Matheny (1989) that highly active children, as rated by their parents, may find it more difficult to attend to appropriate stimulation. No association between cognitive development and SP was observed in this study.

Summarizing, both observed social-communicative symptoms of ASD and observed RRB's were predicted by a temperamental subscale of NA, namely Perceptual Sensitivity. ADOS observations were not predicted by any SP scales. Low Registration was predictive for both social-communicative symptoms of ASD and RRB's, as reported by parents. Parent-reported RRB's were furthermore predicted by another SP scale, namely Auditory SP, while parent-reported social-communicative symptoms were predicted by a temperamental subscale of NA, namely Soothability. Lastly, cognitive development in preterm children was predicted by Activity Level, a temperamental subscale of

Surgency, which was in line with our hypothesis. An overview of the main findings is provided in Table 10. Our hypothesis that different variables may predict parent-reported and observational measures of ASD was also confirmed, and the lack of correlations we found between these measures was in line with previous findings within this field of research (Bishop et al., 2002; de Bildt et al., 2004). However, not all of the subscales we hypothesised to be predictors turned out to actually be predictive. Several reasons might be accountable for this. For instance, some scales from Table 1 (e.g. Activity Level at 24 months) had to be excluded because they were not internally consistent. Temperament was furthermore not always assessed with instruments based on the Rothbart approach in previous studies. It could be that a concept that was measured by two different instruments does not cover exactly the same content and as such was predictive in a previous study but not in this study.

Table 10.
Summary of main findings

	ADOS_SA	SRS_SCI	ADOS_RRB	SRS_RRB	MSEL
Sensory Processing		√		√	
Temperament					
NA	√	√	√		
Surgency					√
EC					

ADOS-2 Autism Diagnostic Observation Schedule-2; *SRS-2* Social Responsiveness Scale-2; *MSEL* Mullen Scales of Early Learning; *SA* Social Affect; *SCI* Social Communication and Interaction, *RRB* Restricted and Repetitive Behaviour; *NA* Negative Affect; *EC* Effortful Control

4.4. Limitations and future directions

A first limitation of this study is the fact that temperament and SP were assessed solely by parent report, which is known to be subject to biases. Furthermore, the correlations that were found between the SRS-2 and the measures of temperament and SP are influenced by shared method variance, as both the SRS-2 and the temperamental and SP questionnaires are parent-reported assessments. However, the fact that parents are familiar with the behaviour of their child in different settings and over a longer period in time makes them a good source of information that should not be replaced, but rather be complemented by the use of multiple informants or observational measures. Second, our sample size was rather small. This, in combination with the fact that some of the temperamental and SP scales had to be excluded or had to be substituted by their subscales due to unsatisfactory internal consistency, prevented us to use all the scales of the temperament and SP questionnaires in our analyses. Moreover, a maximum of four predictors per outcome variable was selected (Harrell, 2001), which limited the conclusions that could be drawn from our analyses. Future research would benefit

from larger samples. Third, given the limited internal consistency of some scales of the ITSP, IBQ-R and ECBQ in this study and given the fact that we cannot assume that instruments that are developed for typically developing children are as useful and valid in atypically developing children, it could be sensible to undertake research focused on the further validation of the ITSP, IBQ-R and ECBQ in children with an atypical development. Lastly, evidence that temperament and SP are related concepts is growing (e.g. Nakagawa et al., 2016). Given this suggested overlap, it could be interesting to perform a factor analysis with all of the items of the temperament and SP questionnaires. This could possibly result in new, more internally consistent scales that moreover might be more informative.

4.5. Conclusion

In this study, temperament at 18 months was predictive for cognitive development at 36 months, while temperament and SP at 18 and 24 months were associated with symptoms of ASD at 36 months. These findings extend similar previous research on the predictive value of temperament and SP in other populations. The results should however be nuanced, as a number of scales – especially the ones in the first year of life – that were predictive in research with other populations, turned out to have no significant predictive value in our study. Given that symptoms of ASD emerge in the second year of life, we have to be careful about considering markers at 18 and 24 months as predictive. When interpreting the results, we should furthermore keep in mind the abovementioned limitations of the study. Moreover, correlational group analyses are not sufficient in terms of prediction of outcome in individual cases. Nevertheless, our data provide a first indication that temperament traits and SP are worth further investigation in the extreme and very preterm population, in order to learn more about whether these two concepts might be able to provide information about which preterms are more likely to develop ASD or cognitive impairments.

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