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Perinatal complications are associated with social anxiety: Indirect effects through temperament

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Abstract

The current investigation examines the relation between perinatal complications and social anxiety incorporating the potential indirect effect of child temperament. Participants were 149 children aged 9 to 12 years (M_{age} = 9.97, SD_{age} = 1.00) screened for behavioural inhibition (BI) and assessed for social anxiety symptoms using parent and child reports. Participating families also reported on the presence of perinatal complications. Results indicated that children who experienced perinatal complications were higher in BI and social anxiety than were children who did not experience complications. Furthermore, there was an indirect effect between perinatal complications and social anxiety via BI. These findings provide further support for the established relation between perinatal complications and anxiety and demonstrate, for the first time, that this relation may be mediated by temperament, setting the stage for longitudinal analyses.

Highlights

- Perinatal complications were associated with increased social anxiety and fearful temperament (i.e., behavioral inhibition).
- The relation between perinatal complications and social anxiety may be mediated by children's fearful temperament.

- Results support the established relation between perinatal complications and anxiety and show that this relation may be mediated by temperament.

KEYWORDS

perinatal complications, social anxiety, temperament

1 | INTRODUCTION

Specific temperamental traits evident early in development predict the emergence of psychopathology later in life. In particular, behavioural inhibition (BI) is a temperament characterized by a tendency to exhibit a fearful disposition and withdrawal in unfamiliar contexts and situations (Kagan, Reznick, Clarke, Snidman, & Garcia-Coll, 1984). Children who strongly and consistently exhibit BI early in life are at increased risk for the development of anxiety symptoms and disorders in childhood and in adolescence, especially social anxiety (Pérez-Edgar & Fox, 2005).

For example, a comprehensive meta-analytic review examined seven longitudinal studies investigating the link between BI in children and social anxiety (Clauss & Blackford, 2012). They found that children identified as behaviourally inhibited are at a threefold to fourfold increased risk for the development of social anxiety disorder. Additionally, a longitudinal study found that adolescents aged 14 to 16 years were 3.79 times more likely to be diagnosed with lifetime social anxiety disorder if they consistently displayed high levels of BI during childhood, based on maternal report (Chronis-Tuscano et al., 2009). Thus, it is essential to identify early developmental risk factors that may be associated with, and could be used as predictors of, BI as a readily observable phenotype for identifying risk for social anxiety disorder. In the current study, we examined perinatal complications as a potential early developmental risk factor associated with both BI and social anxiety. Moreover, we investigated the potential indirect effect of temperament in the relation between perinatal complications and social anxiety, setting the stage for future studies of mediation.

There are many reasons to believe that perinatal complications may impact children's temperament and mental health outcomes. Primarily, there is empirical evidence demonstrating that prenatal, perinatal, and post-natal complications are associated with risk for psychopathology and, specifically, anxiety disorders later in life. For example, Cohen and colleagues (1989) found that pregnancy problems (e.g., low birthweight, physical trauma, severe illness, complications during pregnancy or delivery, and caesarean sections) were significant risk factors for anxiety in children and adolescents. Another study found that parents of children with anxiety disorders reported higher rates of perinatal complications, including preterm birth, than did parents of unaffected children (Johnco et al., 2016). Studies that have investigated the relation between perinatal complications and various forms of psychopathology have found that perinatal complications (e.g., poor maternal obstetric history) appear to be a specific risk for anxiety disorders in offspring, as opposed to externalizing disorders and substance use disorders, which tend to be associated with maternal prenatal substance use (Allen, Lewinsohn, & Seeley, 1998; Essau, Sasagawa, Lewinsohn, & Rohde, 2018).

Furthermore, prenatal and perinatal complications (e.g., heavy bleeding, severe illness, hypertension, or excessive fluid retention) predict risk for childhood anxiety disorders, above and beyond the familial risk of parental psychopathology (Hirshfeld-Becker et al., 2004). In particular, there appeared to be an additive effect, as children who were exposed to multiple prenatal and perinatal complications were at increased risk for anxiety. Finally, a study (Freed et al., 2014) investigated obstetric complications as a mediating factor in the relation between parental lifetime anxiety and child lifetime psychopathology. In this study, children who experienced delivery complications were much more likely to be diagnosed with anxiety disorders. This relation remained significant even after controlling for parental lifetime anxiety disorders.

Associated studies have demonstrated that preterm birth and low birthweight, as specific indicators of perinatal complications, are risk factors for poor socioemotional and personality development. Adults born very preterm (i.e., less than 33 weeks' gestation) were more likely to self-report lower extraversion scores and higher neuroticism scores and exhibited a personality profile characterized by greater negative affect and BI and lower positive affect and sensation seeking than were their term-born counterparts (Allin et al., 2006). In parallel, adults who were born at extremely low birthweight, compared with normal-birthweight adults, are more likely to display a profile of significantly higher shyness and BI (Schmidt, Miskovic, Boyle, & Saigal, 2008). Taken together, these findings highlight possible early developmental risk factors associated with the emergence of distinct temperament and personality profiles. These profiles, in turn, may place individuals at risk for social anxiety and other mental health issues, starting very early in development. There is empirical evidence to demonstrate that early neonatal events, such as low birthweight, confer a twofold to fourfold increase in offspring's risk for anxiety disorders (Nomura et al., 2007).

Finally, associated biological mechanisms further support a relation between perinatal experiences and early temperament. The perinatal period is thought to be a crucial period of development during which the stress-regulation systems of the body are adjusted and finely tuned (Van Den Bergh, 2011). As such, experiences during this period may lead to biological changes that produce lasting effects into later development, impacting physical and mental health outcomes. Animal models, for example, suggest that prenatal and perinatal stressors are associated with later sensitivity to novelty and BI-like behaviours, potentially mediated by permutations in glucocorticoid functioning (Cavigelli, 2018; Tang, Reeb-Sutherland, Romeo, & McEwen, 2012). Preliminary data in humans also suggest that exposure to prenatal stress may increase infant fearfulness, particularly in females, via epigenetic modification of the glucocorticoid receptor gene (Ostlund et al., 2016).

The studies outlined thus far suggest that perinatal complications are potential early developmental risk factors associated with poor emotional regulation and difficult temperament in infants, children, and adolescents. To our knowledge, there is no research examining the relation between perinatal complications, temperament, and anxiety in childhood. These are important areas to explore, as prior research provides robust evidence demonstrating the importance of early experience and perinatal development and their effects on neurological and behavioural development. Our study aimed to leverage a large-scale study of BI as an initial assessment of the relation between perinatal complications, temperament, and social anxiety. In particular, we evaluated if BI acts as a potential mediating factor between perinatal complications and the presence of social anxiety symptoms in childhood, by first exploring the indirect effects evident in the current sample.

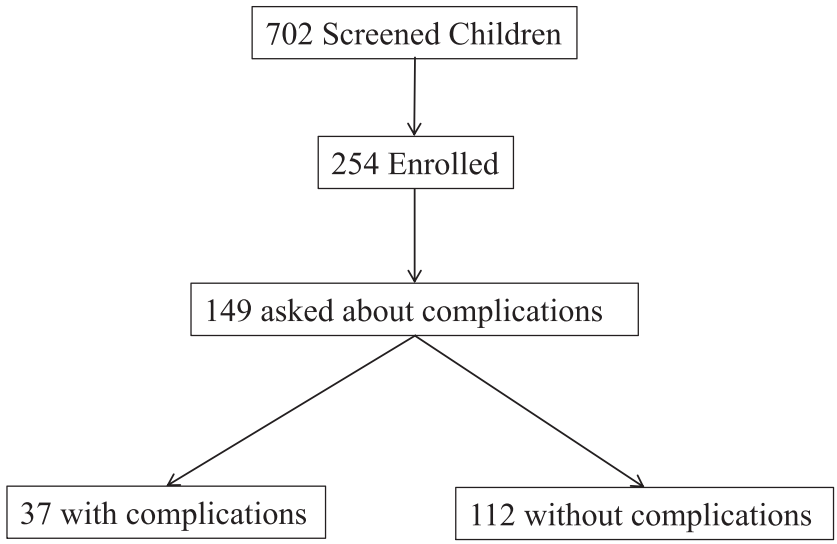

FIGURE 1 Diagram illustrating the sampling strategy for the current study

2 | METHODS

2.1 | Participants

The current analysis drew from a larger laboratory study of temperament, attention, and anxiety. Data were collected from May 2012 to December 2016. Figure 1 illustrates the sampling strategy for the current study. We screened 702 children aged 9–12 years (M_{age} = 9.97, SD_{age} = 1.00, 365 male) for participation in the laboratory study using parental report on the Behavioral Inhibition Questionnaire (BIQ; Bishop, Spence, & McDonald, 2003). Children who met preset cut-off scores (≥119 total score or ≥60 social novelty subscale) were identified as BI (*N* = 130, 18.5%). Cut-off scores were based on a previous study of extreme temperament in children aged 4 to 15 years (Broeren & Muris, 2010). The fully screened sample was 89.9% Caucasian, 2.0% African American, 2.0% Hispanic, 1.3% Asian, 4.0% biracial, and 1.0% declined to respond.

Over the course of the screening process, we noted verbal reports of birth complications from parents already enrolled in the study. As such, we added questions probing the early medical history of the potential participants, including the presence of perinatal birth complications. Of the full screening sample, 379 families (54.0%) were asked about complications. This subset of families did not differ from the remaining screening sample on core study variables (*p*s > 0.65).

Screened families were asked two yes/no questions probing if their child was born more than 2 weeks from the due date and if the child experienced birth complications. An additional open-ended question then allowed parents to describe the nature of the complications. From these responses, we removed answers that did not fit the parameters of perinatal complications (e.g., child has a subsequent food allergy). As expected, we found a wide range of concerns, and many participants experienced multiple complications (e.g., low birthweight and neonatal intensive care unit admission). The most common complications were breech birth (16.2%), neonatal intensive care unit admission (16.2%), cardiopulmonary distress (16.2%), maternal distress during or after pregnancy/labour (16.2%), unplanned caesarean section (13.5%), gastrointestinal complications (8.1%), and perinatal surgery (8.1%). Although this measure relies on self-reported perinatal complications, research has shown that retrospective reports of perinatal events have moderate to high validity, especially among well-educated mothers (Bat-Erdene, Metcalfe, McDonald, & Tough, 2013; Buka, Goldstein, Spartos, & Tsuang, 2004; Coolman et al., 2010; Neiderhiser et al., 2016).

On the basis of the full sample screen, we invited behaviourally inhibited children to enrol in the larger laboratory study of temperament, attention, and anxiety (e.g., Morales, Taber-Thomas, & Pérez-Edgar, 2017; Thai, Taber-Thomas, & Pérez-Edgar, 2016). Noninhibited children were also invited to enrol as nonyoked age- and gender-matched controls to the behaviourally inhibited children. In total, 254 children enrolled in the larger study (Figure 1). The enrolled sample was enriched for BI, such that 88 children (34.6%) met the BI criteria and 166 children were non-BI. Enrolled parents

TABLE 1 Demographic characteristics and descriptive statistics (mean and standard deviation) of main study variables

		Birth complications	
Measures	**Full sample**	**Yes**	**No**
N	149	37	112
Gender	77 M/72 F	18 M/19 F	59 M/53 F
Age	9.99 (0.93)	10.14 (0.98)	9.95 (0.92)
Total BIQ	95.19 (32.90)	114.00 (31.96)**	88.98 (30.92)**
Parent-report social anxiety	1.69 (3.07)	3.38 (3.79)**	1.13 (2.58)**
Child-report social anxiety	3.01 (3.46)	3.51 (3.29)	2.84 (3.51)

Note. BIQ: Behavioral Inhibition Questionnaire.

*p < 0.05. **p < 0.01. ***p < 0.10.

and children were interviewed regarding the child's social anxiety symptoms using the Diagnostic Interview Schedule for Children Version IV (C-DISC 4; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000).

In total, 149 children had available data on BI level, perinatal complications, and both parent and child reports of social anxiety for the current analysis (Table 1; Figure 1). Although the children included in this analysis did not differ from the screened, but excluded, children on demographic variables (*ps* > 0.43), there was a significant increase in BI level ($M_{included}$ = 95.2 vs. $M_{excluded}$ = 89.2, p = 0.04) because we specifically enriched the sample on this variable.

Screened families were recruited using the university's database of families interested in participating in research studies, community outreach, and word-of-mouth throughout the region surrounding State College, PA. All parents and children provided written consent/assent. Participants received monetary compensation for completing the screening questionnaires and additional compensation for participating in the larger study once enrolled. All recruitment and study methods were approved by the institutional review board of The Pennsylvania State University.

2.2 | Measures

Parents completed the BIQ (Bishop et al., 2003), a 30-item questionnaire consisting of BI-linked behaviour in the domains of social and situational novelty assessed on a 7-point Likert scale. The questionnaire has adequate internal consistency and validity in differentiating children with or without BI (Bishop et al., 2003), and parental reports on the BIQ are correlated with laboratory observations of BI (Dyson, Klein, Olino, Dougherty, & Durbin, 2011). In the present study, the BIQ had good internal consistency (α = 0.86). Continuous total BIQ scores were used for our analyses (range = 30–165).

To assess social anxiety symptoms, the computer-assisted C-DISC 4 (Shaffer et al., 2000) was administered separately to primary caregivers and the child participants. The C-DISC 4 is a widely used, reliable, and well-validated measure of anxiety symptoms and disorders with strong test–retest reliability (Shaffer et al., 2000; Silverman, Saavedra, & Pina, 2001). A trained research assistant conducted the semistructured interview, in which participants judged *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, symptoms as either present (yes) or absent (no). Sample questions from C-DISC 4 Question for Social Anxiety include "In the last year—that is, since you started fifth grade—was there a time when you felt worried about speaking out loud in class?" and "In the past year have you been very concerned with being liked by others?" Yes responses were tallied to obtain a total symptom score. Total symptom scores ranged from 0 to 12, for both primary caregivers and children. In addition, the C-DISC also asks for symptom frequency, duration, and impairment in order to assess clinical criteria. The series of

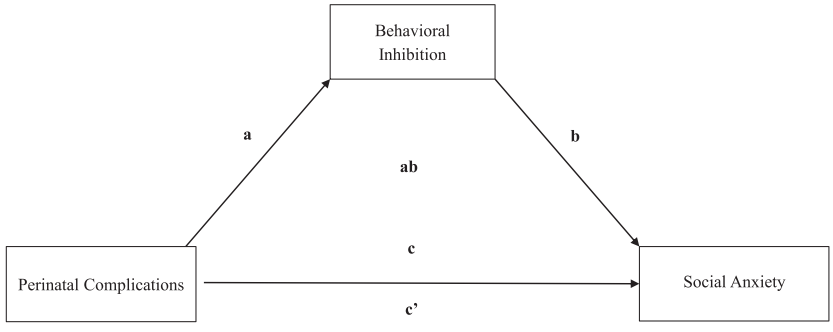

FIGURE 2 Conceptual diagram illustrating the mediation model used to test the relations between perinatal complications, BI, and social anxiety symptoms. *a*: Direct effect perinatal complications on behavioural inhibition; *b*: direct effect of behavioural inhibition on social anxiety; *ab*: indirect effect of perinatal complications on social anxiety via the effect on behavioural; *c*: total effect of perinatal complications on social anxiety; *c′*: direct effect of perinatal complications on social anxiety. BI: behavioural inhibition

impairment questions are incorporated at the end of each diagnostic section only if a clinically significant number of symptoms have already been endorse, usually half or more of those required for the diagnosis. Research assistants conducting the interviews all had bachelor's or master's degrees and were trained by a researcher with a master's degree in clinical psychology.

2.3 | Model testing

We tested a mediation model (Hayes, 2013; Preacher, Rucker, & Hayes, 2007) to assess the relations between perinatal complications, BI, and social anxiety (see Table 4; Figure 2) using SPSS (Version 24; Chicago, IL) PROCESS Model 4. Models were run separately for parent report and child self-report of symptom presentation. Continuous variables were mean centred prior to analysis. Significant conditional indirect effects were determined using 95% bootstrap bias-corrected confidence intervals based on 10,000 bootstrap samples.

The specific models tested here were derived from the available literature in adults (Allin et al., 2006; Schmidt et al., 2008) and our theoretical assumptions regarding the temporal chain between perinatal stress, temperament, and anxiety symptoms. Given that only a relative minority of children experienced birth complications in the final sample, we utilized a model that is robust to differences in group sample size based on the bootstrapping procedure, which provides a representation of the sampling distribution of the indirect effect (Hayes & Rockwood, 2017). Initial analyses included age and sex as covariates in the model. However, we found no systematic effects for either variable, and they did not impact the larger indirect effect. They were then removed for parsimony.

3 | RESULTS

In the current analyses, 37 children (24.8%) experienced perinatal complications (Tables 1 and 2). Perinatal complication status did not differ with age or gender ($ps > 0.29$). Children experiencing perinatal complications were higher in BI, $t(147) = -4.23$, $p < 0.001$, $d = 0.70$, and had more social anxiety symptoms based on parent-report symptoms, $t(147) = -4.06$, $p < 0.001$, $d = 0.67$. Although in the same direction, the effect of perinatal complications was not significant for child-report symptoms, $t(147) = -1.03$, $p = 0.31$, $d = 0.17$. As expected, we found significant intercorrelations between BI scores, parent-report symptoms, and child-report symptoms (Table 3).

TABLE 2 Distribution of diagnostic assessments of social anxiety with the DISC for participants as a function of BI status and report of complications

	Parent report				Child report			
	Complications		No complications		Complications		No complications	
Anxiety category	BI	Non-BI	BI	Non-BI	BI	Non-BI	BI	Non-BI
Low anxiety	13	10	26	72	14	7	20	58
Subthreshold anxiety	10	2	8	3	8	5	14	14
Clinical anxiety	2	0	3	0	3	0	3	3

Note. Diagnostic categories are determined by the DISC based on a combination of symptom counts, duration, and frequency, as well as level of impairment. Impairment levels are assessed if the child or parent has endorsed half or more of the queried symptoms. For diagnosis, the symptom disturbance must be evident for 6 months or longer and has caused significant distress. The distribution of complications and diagnosis by BI group was significant for both caregivers, $X^2(2) = 24.11$, $p < 0.001$, and children, $X^2(2) = 6.93$, $p = 0.031$. BI and non-BI categorization for this table was based on the initial parental screening with the BIQ. BI children had cut-off scores ≥ 119 for the total score or ≥ 60 for the social novelty subscale. Continuous BIQ scores were used in all of the presented analyses. BI: behavioural inhibition; BIQ: Behavioral Inhibition Questionnaire; DISC: Diagnostic Interview Schedule for Children.

TABLE 3 Bivariate correlations for perinatal complications, BIQ score, social anxiety symptoms, and age

	Complications	BI	Parent report	Child report	Age	Gender
Complications	—					
BI	0.330**	—				
Parent report	0.318**	0.514**	—			
Child report	0.085	0.225**	0.295**	—		
Age	0.088	−0.053	0.106	0.048	—	
Gender	0.035	0.102	0.178*	0.197*	0.223**	—

Note. Complications (0 = absent, 1 = present), gender (0 = male, 1 = female), and total $N = 149$. BI: behavioural inhibition; BIQ: Behavioral Inhibition Questionnaire.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.10$.

3.1 | Perinatal complications, BI, and parent-report social anxiety

As shown in Table 4, the model (Figure 2) found that the significant association between perinatal complications and social anxiety (*c*) is explained through BI. The paths were significant from perinatal complications to BI (*a*) and from BI to social anxiety symptoms (*b*). Importantly, the indirect effect of perinatal complications on social anxiety through BI was significant (*ab*). The direct effect of perinatal complications on social anxiety symptoms (*c′*) was also significant.

3.2 | Perinatal complications, BI, and self-report social anxiety

The model found that the total association between perinatal complications and social anxiety (*c*) was not significant (Table 4). Here, the direct effect of perinatal complications on social anxiety symptoms (*c′*) was not significant.

TABLE 4 Path results for the mediation models for parent-report and child self-report of child social anxiety

Outcome Measure	Path Tested	Unstandardized coefficient	Standard error	*t*	*p*	LLCI	ULCI
Parent report of child anxiety	PC→SA *c*	2.25	0.55	4.06	0.000	1.158	3.349
	PC→BI *a*	25.02	5.91	4.23	0.000	13.341	36.697
	BI→SA *b*	0.04	0.01	6.22	0.000	0.029	0.057
	PC→SA *c′*	1.18	0.52	2.25	0.026	0.143	2.214
	PC→BI→SA *ab*	1.07	0.27	—	—	0.560	1.629
Child report of child anxiety	PC→SA *c*	0.67	0.66	1.03	0.305	−0.620	1.969
	PC→BI *a*	25.02	5.91	4.23	0.000	13.341	36.697
	BI→SA *b*	0.02	0.01	2.59	0.011	0.006	0.041
	PC→SA *c′*	0.09	0.68	0.14	0.892	−1.253	1.438
	PC→BI→SA *ab*	0.58	0.27	—	—	0.114	1.175

Note. BI: behavioural inhibition; LLCI: lower level confidence interval; PC: perinatal complications; SA: social anxiety; ULCI: upper level confidence interval.

However, the paths were again significant from perinatal complications to BI (*a*) and from BI to social anxiety symptoms (*b*). As with parent report, the test of indirect effects was significant for perinatal complications on social anxiety through BI (*ab*).

4 | DISCUSSION

In the current study, we sought to evaluate perinatal complications as possible early developmental risk factors associated with BI and social anxiety. In addition, we examined BI as an indirect path that could help explain the relation between perinatal complications and the presence of social anxiety symptoms later in life. Our results suggest that perinatal complications may be associated with a broad pattern of development that underscores known risk factors for anxiety. These findings are in line with a broader literature linking the earliest days of life to long-term patterns of psychosocial functioning (Freed et al., 2014; Hirshfeld-Becker et al., 2004; Pollak et al., 2010). Although preliminary, the current study provides support for follow-up studies targeting specific perinatal complications and socioemotional function over time in childhood.

Our findings are consistent with those of prior studies reporting associations between perinatal complications and risk for childhood anxiety disorders (Cohen, Velez, Brook, & Smith, 1989; Freed et al., 2014; Hirshfeld-Becker et al., 2004; Johnco et al., 2016). We extend these findings, highlighting a specific relation between perinatal complications and risk for social anxiety symptoms in children. However, we found that the direct relation between perinatal complications and social anxiety symptoms was significant for the parent-report model but did not reach statistical thresholds for the child self-report model, albeit in the same direction. Finding inconsistent results across informants is not uncommon (De Los Reyes & Kazdin, 2005; De Los Reyes, Thomas, Goodman, & Kundey, 2013).

One possible explanation for this discrepancy could be that there is a stronger relation for the parents because the parent is the informant for both perinatal complications and child social anxiety symptomology. Events surrounding, and then subsequent to, the perinatal complications may colour the parent's view of the child's functioning. Moreover, parents and children may be assessing and understanding symptoms of anxiety differently. Prior research suggests that parent and child agreement is generally lower for anxiety disorders (Barbosa, Tannock, & Manassis, 2002). In line with this literature, we find a significant but modest correlation between parent and child reports ($r = 0.30$), suggesting considerable unique variance for each informant. Given that there is no "gold standard" measure for psychopathology and each informant provides unique information, it is important for future studies to incorporate multiple informants (De Los Reyes & Kazdin, 2005).

Despite the lack of statistical consistency between the parent- and self-report models, the indirect effect of temperament is similar for both models. Specifically, we find that perinatal complications are associated with higher levels of BI and that this temperament trait is related to increased social anxiety. Our findings are unique in that both the parent- and self-report models indicate that BI is an underlying factor linking the relation between perinatal complications and social anxiety symptoms. This result is in line with studies in adults that find that poor obstetric outcomes, such as low birthweight and preterm birth, are associated with less adaptive socioemotional and personality development, typically characterized by low extraversion, higher shyness, and BI (Allin et al., 2006; Schmidt et al., 2008). Furthermore, obstetric complications and preterm birth seem to be more strongly associated with anxiety disorders (Essau et al., 2018; Freed et al., 2014), especially when coupled with other risk factors (e.g., maternal hostility; Neiderhiser et al., 2016). In contrast, other factors, such as maternal substance use during pregnancy (e.g., smoking), are more strongly related to externalizing and attention problems (Wakschlag et al., 1997; Weissman, Warner, Wickramaratne, & Kandel, 1999).

Although our study does make an important contribution, lending support to the proposition that child temperament may be one of the underlying developmental processes linking perinatal complications and social anxiety symptoms, it is difficult to rule out other potential contributing factors.

First, our study did not assess characteristics of the mother. Thus, we were unable to consider how maternal psychological factors may affect the child at different stages of development. Independent studies have found that

prenatal maternal stress is a predictor of both perinatal complications (Copper et al., 1996; Dunkel-Schetter, 1998; Lou et al., 1994; Sandman, Davis, & Glynn, 2012) and child temperament (Blair, Glynn, Sandman, & Davis, 2011; Gutteling et al., 2005; Huizink, De Medina, Mulder, Visser, & Buitelaar, 2002; Huttenen, Martin, Noyes, Wisenbaker, & Huttunen, 1999; O'Connor, Heron, Golding, Beveridge, & Glover, 2002). For example, maternal stress during pregnancy has been associated with smaller head circumference at birth, perhaps indicating variations in foetal brain development (Lou et al., 1994). It is also well established that maternal stress during pregnancy is correlated with spontaneous preterm delivery and low birthweight (Copper et al., 1996; Dunkel-Schetter, 1998; Sandman et al., 2012). Beyond obstetric markers, maternal levels of perceived stress during pregnancy are also associated with increased negative affect and emotional and behavioural problems from infancy to childhood (Blair et al., 2011; Gutteling et al., 2005; Huizink et al., 2002; Huttenen et al., 1999; O'Connor et al., 2002).

Thorough assessment of maternal characteristics would also allow future studies to account for the possible influence of the post-natal environment. For instance, both maternal anxiety and perinatal complications may be risk factors for maternal post-partum psychopathology. Prior studies indicate that maternal antenatal anxiety predicts post-natal depression and anxiety and that the experience of severe obstetric complications is associated with more intense post-natal depressive symptoms, independent of prior anxiety or depression diagnoses (Coelho, Murray, Royal-Lawson, & Cooper, 2011; Heron et al., 2004; Verdoux, Sutter, Glatigny-Dallay, & Minisini, 2002). Maternal post-partum depression and anxiety may indirectly increase the risk for child psychopathology by affecting mother–child interactions. Thus, future studies should carefully consider maternal traits and characteristics both prepartum and post-partum in order to understand how these factors may uniquely impact the development of child social anxiety symptoms.

Second, the oversampling of behaviourally inhibited children may limit the generalizability of our findings. Thus, this study should not be utilized as an index for the prevalence of BI and/or perinatal complications. Third, the retrospective self-reporting of perinatal complications is an additional limitation of this study, as mothers may not be able to clearly recall events that occurred during pregnancy and delivery. Future studies should consider examining the relation between perinatal complications, early temperament, and psychopathology using prospective, longitudinal methods. To the best of our knowledge, most studies that have investigated the relation between perinatal complications and anxiety disorders in children do so concurrently and use maternal retrospective report of perinatal complications (for an exception, see Neiderhiser et al., 2016). This allows for many forms of shared method variance. It is difficult to determine the accuracy of the mother's recollections of the events that occurred during and before birth, and it is possible that mothers with anxiety disorders may be prone to recall more problems during their pregnancies. However, past studies demonstrate that maternal recollection of birth complications is valid particularly for complications like the ones described in this study and among highly educated families (Bat-Erdene et al., 2013; Buka et al., 2004; Coolman et al., 2010; Neiderhiser et al., 2016). Future studies should carefully measure maternal traits and characteristics, incorporate multiple informants, and include behavioural measures for temperament assessment.

Despite these limitations, our study offers important insight as it shows, for the first time in children, that perinatal complications are associated with fearful temperament and may be an early risk factor for social anxiety. Moreover, our findings provide initial evidence that temperament may be one of the underlying developmental processes linking perinatal complications and anxiety. Our findings are in line with the broader literature suggesting that stressors occurring during the perinatal period of development can critically impact neural and behavioural development (Bock, Rether, Gröger, Xie, & Braun, 2014), particularly as expressed in reactive temperamental profiles (Lin, Ostlund, Conradt, Lagasse, & Lester, 2018). Thus, investigating structural and functional abnormalities in brain areas associated with the regulation and mediation of emotionality may provide a more direct link between early life stressors and the later emergence of behavioural problems and psychopathology. Further investigation into the relation between perinatal complications, early temperament, and social anxiety is important in that the findings provide the opportunity to identify and target potential underlying mechanisms, providing new insight into how to more effectively prevent or address the potential consequences of perinatal complications.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

Allen, N. B., Lewinsohn, P. M., & Seeley, J. R. (1998). Prenatal and perinatal influences on risk for psychopathology in childhood and adolescence. *Development and Psychopathology*, *10*(3), 513–529. https://doi.org/10.1017/S0954579498001722

Allin, M., Rooney, M., Cuddy, M., Wyatt, J., Walshe, M., Rifkin, L., & Murray, R. (2006). Personality in young adults who are born preterm. *Pediatrics*, *117*(2), 309–316. https://doi.org/10.1542/peds.2005-0539

Barbosa, J., Tannock, R., & Manassis, K. (2002). Measuring anxiety: Parent–child reporting differences in clinical samples. *Depression and Anxiety*, *15*(2), 61–65. https://doi.org/10.1002/da.10022

Bat-Erdene, U., Metcalfe, A., McDonald, S. W., & Tough, S. C. (2013). Validation of Canadian mothers' recall of events in labour and delivery with electronic health records. *BMC Pregnancy and Childbirth*, *13*(1), S3. https://doi.org/10.1186/1471-2393-13-S1-S3

Bishop, G., Spence, S. H., & McDonald, C. (2003). Can parents and teachers provide a reliable and valid report of behavioral inhibition? *Child Development*, *74*(6), 1899–1917. https://doi.org/10.1046/j.1467-8624.2003.00645.x

Blair, M. M., Glynn, L. M., Sandman, C. A., & Davis, E. P. (2011). Prenatal maternal anxiety and early childhood temperament. *Stress*, *14*(6), 644–651. https://doi.org/10.3109/10253890.2011.594121

Bock, J., Rether, K., Gröger, N., Xie, L., & Braun, K. (2014). Perinatal programming of emotional brain circuits: An integrative view from systems to molecules. *Frontiers in Neuroscience*, *8*, 11.

Broeren, S., & Muris, P. (2010). A psychometric evaluation of the behavioral inhibition questionnaire in a non-clinical sample of Dutch children and adolescents. *Child Psychiatry & Human Development*, *41*(2), 214–229. https://doi.org/10.1007/s10578-009-0162-9

Buka, S. L., Goldstein, J. M., Spartos, E., & Tsuang, M. T. (2004). The retrospective measurement of prenatal and perinatal events: Accuracy of maternal recall. *Schizophrenia Research*, *71*(2–3), 417–426. https://doi.org/10.1016/j.schres.2004.04.004

Cavigelli, S. A. (2018). Behavioral inhibition in rodents: A model to study causes and health consequences of temperament. In *Behavioral inhibition* (pp. 35–58). Cham, Switzerland: Springer.

Chronis-Tuscano, A., Degnan, K. A., Pine, D. S., Perez-Edgar, K., Henderson, H. A., Diaz, Y., … Fox, N. A. (2009). Stable early maternal report of behavioral inhibition predicts lifetime social anxiety disorder in adolescence. *Journal of the American Academy of Child & Adolescent Psychiatry*, *48*(9), 928–935. https://doi.org/10.1097/CHI.0b013e3181ae09df

Clauss, J. A., & Blackford, J. U. (2012). Behavioral inhibition and risk for developing social anxiety disorder: A meta-analytic study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *51*(10), 1066–1075. https://doi.org/10.1016/j.jaac.2012.08.002

Coelho, H. F., Murray, L., Royal-Lawson, M., & Cooper, P. J. (2011). Antenatal anxiety disorder as a predictor of postnatal depression: A longitudinal study. *Journal of Affective Disorders*, *129*(1–3), 348–353. https://doi.org/10.1016/j.jad.2010.08.002

Cohen, P., Velez, C. N., Brook, J., & Smith, J. (1989). Mechanisms of the relation between perinatal problems, early childhood illness, and psychopathology in late childhood and adolescence. *Child Development*, *60*, 701–709. https://doi.org/10.2307/1130735

Coolman, M., de Groot, C. J., Jaddoe, V. W., Hofman, A., Raat, H., & Steegers, E. A. (2010). Medical record validation of maternally reported history of preeclampsia. *Journal of Clinical Epidemiology*, *63*(8), 932–937. https://doi.org/10.1016/j.jclinepi.2009.10.010

Copper, R. L., Goldenberg, R. L., Das, A., Elder, N., Swain, M., Norman, G., … Jones, P. (1996). The preterm prediction study: Maternal stress is associated with spontaneous preterm birth at less than thirty-five weeks' gestation. *American Journal of Obstetrics and Gynecology*, *175*(5), 1286–1292. https://doi.org/10.1016/S0002-9378(96)70042-X

De Los Reyes, A., & Kazdin, A. E. (2005). Informant discrepancies in the assessment of childhood psychopathology: A critical review, theoretical framework, and recommendations for further study. *Psychological Bulletin*, *131*(4), 483–509. https://doi.org/10.1037/0033-2909.131.4.483

De Los Reyes, A., Thomas, S. A., Goodman, K. L., & Kundey, S. M. (2013). Principles underlying the use of multiple informants' reports. *Annual Review of Clinical Psychology*, *9*, 123–149. https://doi.org/10.1146/annurev-clinpsy-050212-185617

Dunkel-Schetter, C. (1998). Maternal stress and preterm delivery. *Prenatal and Neonatal Medicine*, *3*, 39–42.

Dyson, M. W., Klein, D. N., Olino, T. M., Dougherty, L. R., & Durbin, C. E. (2011). Social and non-social behavioral inhibition in preschool-age children: Differential associations with parent-reports of temperament and anxiety. *Child Psychiatry & Human Development*, *42*(4), 390–405. https://doi.org/10.1007/s10578-011-0225-6

Essau, C. A., Sasagawa, S., Lewinsohn, P. M., & Rohde, P. (2018). The impact of pre- and perinatal factors on psychopathology in adulthood. *Journal of Affective Disorders*, *236*, 52–59. https://doi.org/10.1016/j.jad.2018.04.088

Freed, R. D., Tompson, M. C., Otto, M. W., Nierenberg, A. A., Hirshfeld-Becker, D., Wang, C. H., & Henin, A. (2014). Early risk factors for psychopathology in offspring of parents with bipolar disorder: The role of obstetric complications and maternal comorbid anxiety. *Depression and Anxiety*, *31*(7), 583–590. https://doi.org/10.1002/da.22254

Gutteling, B. M., de Weerth, C., Willemsen-Swinkels, S. H., Huizink, A. C., Mulder, E. J., Visser, G. H., & Buitelaar, J. K. (2005). The effects of prenatal stress on temperament and problem behavior of 27-month-old toddlers. *European Child & Adolescent Psychiatry*, *14*(1), 41–51. https://doi.org/10.1007/s00787-005-0435-1

Hayes A. F. (2013). Introduction to mediation, moderation, and conditional process analysis: A regression-based approach. New York, NY: The Guilford Press. *Journal of Educational Measurement*, *51*(3), 335–337. https://doi.org/10.1111/jedm.12050

Hayes, A. F., & Rockwood, N. J. (2017). Regression-based statistical mediation and moderation analysis in clinical research: Observations, recommendations, and implementation. *Behaviour Research and Therapy*, *98*, 39–57. https://doi.org/10.1016/j.brat.2016.11.001

Heron, J., O'Connor, T. G., Evans, J., Golding, J., Glover, V., & Team, A. S. (2004). The course of anxiety and depression through pregnancy and the postpartum in a community sample. *Journal of Affective Disorders*, *80*(1), 65–73. https://doi.org/10.1016/j.jad.2003.08.004

Hirshfeld-Becker, D. R., Biederman, J., Faraone, S. V., Robin, J. A., Friedman, D., Rosenthal, J. M., & Rosenbaum, J. F. (2004). Pregnancy complications associated with childhood anxiety disorders. *Depression and Anxiety*, *19*(3), 152–162. https://doi.org/10.1002/da.20007

Huizink, A. C., De Medina, P. G. R., Mulder, E. J., Visser, G. H., & Buitelaar, J. K. (2002). Psychological measures of prenatal stress as predictors of infant temperament. *Journal of the American Academy of Child & Adolescent Psychiatry*, *41*(9), 1078–1085. https://doi.org/10.1097/00004583-200209000-00008

Huttenen, M. O., Martin, R. P., Noyes, J., Wisenbaker, J., & Huttunen, M. O. (1999). Prediction of early childhood negative emotionality and inhibition from maternal distress during pregnancy. *Merrill-Palmer Quarterly (1982-)*, *45*(3), 370–391.

Johnco, C., Lewin, A. B., Salloum, A., Murphy, T. K., Crawford, E. A., Dane, B. F., … Storch, E. A. (2016). Adverse prenatal, perinatal and neonatal experiences in children with anxiety disorders. *Child Psychiatry & Human Development*, *47*(2), 317–325. https://doi.org/10.1007/s10578-015-0569-4

Kagan, J., Reznick, J. S., Clarke, C., Snidman, N., & Garcia-Coll, C. (1984). Behavioral inhibition to the unfamiliar. *Child Development*, *55*, 2212–2225. https://doi.org/10.2307/1129793

Lin, B., Ostlund, B. D., Conradt, E., Lagasse, L. L., & Lester, B. M. (2018). Testing the programming of temperament and psychopathology in two independent samples of children with prenatal substance exposure. *Development and Psychopathology*, *30*(3), 1023–1040. https://doi.org/10.1017/S0954579418000391

Lou, H. C., Hansen, D., Nordentoft, M., Pryds, O., Jensen, F., Nim, J., & Hetnmingsen, R. (1994). Prenatal stressors of human life affect fetal brain development. *Developmental Medicine & Child Neurology*, *36*(9), 826–832.

Morales, S., Taber-Thomas, B. C., & Pérez-Edgar, K. E. (2017). Patterns of attention to threat across tasks in behaviorally inhibited children at risk for anxiety. *Developmental Science*, *20*(2), e12391. https://doi.org/10.1111/desc.12391

Neiderhiser, J. M., Marceau, K., Araujo-Greecher, M. D., Ganiban, J. M., Mayes, L. C., … Leve, L. D. (2016). Estimating the roles of genetic risk, perinatal risk, and marital hostility on early childhood adjustment: Medical records and self-reports. *Behavior Genetics*, *46*(3), 334–352. https://doi.org/10.1007/s10519-016-9788-0

Nomura, Y., Wickramaratne, P. J., Pilowsky, D. J., Newcorn, J. H., Bruder-Costello, B., Davey, C., … Weissman, M. M. (2007). Low birth weight and risk of affective disorders and selected medical illness in offspring at high and low risk for depression. *Comprehensive Psychiatry*, *48*(5), 470–478. https://doi.org/10.1016/j.comppsych.2007.04.005

O'Connor, T. G., Heron, J., Golding, J., Beveridge, M., & Glover, V. (2002). Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years: Report from the Avon Longitudinal Study of Parents and Children. *The British Journal of Psychiatry*, *180*(6), 502–508. https://doi.org/10.1192/bjp.180.6.502

Ostlund, B. D., Conradt, E., Crowell, S. E., Tyrka, A. R., Marsit, C. J., & Lester, B. M. (2016). Prenatal stress, fearfulness, and the epigenome: Exploratory analysis of sex differences in DNA methylation of the glucocorticoid receptor gene. *Frontiers in Behavioral Neuroscience*, *10*, 147.

Pérez-Edgar, K., & Fox, N. A. (2005). Temperament and anxiety disorders. *Child and Adolescent Psychiatric Clinics*, *14*(4), 681–706. https://doi.org/10.1016/j.chc.2005.05.008

Pollak, S. D., Nelson, C. A., Schlaak, M. F., Roeber, B. J., Wewerka, S. S., Wiik, K. L., … Gunnar, M. R. (2010). Neurodevelopmental effects of early deprivation in postinstitutionalized children. *Child Development*, *81*(1), 224–236. https://doi.org/10.1111/j.1467-8624.2009.01391.x

Preacher, K. J., Rucker, D. D., & Hayes, A. F. (2007). Addressing moderated mediation hypotheses: Theory, methods, and prescriptions. *Multivariate Behavioral Research*, *42*(1), 185–227. https://doi.org/10.1080/00273170701341316

Sandman, C. A., Davis, E. P., & Glynn, L. M. (2012). Psychobiological stress and preterm birth. In *Preterm birth-mother and child*. Rijeka, Croatia: InTech.

Schmidt, L. A., Miskovic, V., Boyle, M. H., & Saigal, S. (2008). Shyness and timidity in young adults who were born at extremely low birth weight. *Pediatrics*, *122*(1), e181–e187. https://doi.org/10.1542/peds.2007-3747

Shaffer, D., Fisher, P., Lucas, C. P., Dulcan, M. K., & Schwab-Stone, M. E. (2000). NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): Description, differences from previous versions, and reliability of some common diagnoses. *Journal of the American Academy of Child & Adolescent Psychiatry*, *39*(1), 28–38. https://doi.org/10.1097/00004583-200001000-00014

Silverman, W. K., Saavedra, L. M., & Pina, A. A. (2001). Test–retest reliability of anxiety symptoms and diagnoses with the Anxiety Disorders Interview Schedule for DSM-IV: Child and parent versions. *Journal of the American Academy of Child & Adolescent Psychiatry*, *40*(8), 937–944. https://doi.org/10.1097/00004583-200108000-00016

Tang, A. C., Reeb-Sutherland, B. C., Romeo, R. D., & McEwen, B. S. (2012). Reducing behavioral inhibition to novelty via systematic neonatal novelty exposure: The influence of maternal hypothalamic–pituitary–adrenal regulation. *Biological Psychiatry*, *72*(2), 150–156. https://doi.org/10.1016/j.biopsych.2012.03.021

Thai, N., Taber-Thomas, B. C., & Pérez-Edgar, K. E. (2016). Neural correlates of attention biases, behavioral inhibition, and social anxiety in children: An ERP study. *Developmental Cognitive Neuroscience*, *19*, 200–210. https://doi.org/10.1016/j.dcn.2016.03.008

Van Den Bergh, B. R. (2011). Developmental programming of early brain and behaviour development and mental health: A conceptual framework. *Developmental Medicine & Child Neurology*, *53*, 19–23. https://doi.org/10.1111/j.1469-8749.2011.04057.x

Verdoux, H., Sutter, A. L., Glatigny-Dallay, E., & Minisini, A. (2002). Obstetrical complications and the development of postpartum depressive symptoms: A prospective survey of the MATQUID cohort. *Acta Psychiatrica Scandinavica*, *106*(3), 212–219. https://doi.org/10.1034/j.1600-0447.2002.02398.x

Wakschlag, L. S., Lahey, B. B., Loeber, R., Green, S. M., Gordon, R. A., & Leventhal, B. L. (1997). Maternal smoking during pregnancy and the risk of conduct disorder in boys. *Archives of General Psychiatry*, *54*(7), 670–676. https://doi.org/10.1001/archpsyc.1997.01830190098010

Weissman, M. M., Warner, V., Wickramaratne, P. J., & Kandel, D. B. (1999). Maternal smoking during pregnancy and psychopathology in offspring followed to adulthood. *Journal of the American Academy of Child & Adolescent Psychiatry*, *38*(7), 892–899. https://doi.org/10.1097/00004583-199907000-00020

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