



## Social responsiveness in families with parental schizophrenia or bipolar disorder—The Danish High Risk and Resilience Study

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### ABSTRACT

Schizophrenia and bipolar disorder are highly heritable severe mental disorders associated with social impairments. Moreover, partners to individuals with one of these disorders display poorer functioning and more psychopathology, but their social skills and the transgenerational transmission remains uninvestigated. Therefore, we aimed to examine social responsiveness in families with parental schizophrenia or bipolar disorder. The cohort consists of 11-year-old children with at least one parent with schizophrenia ( $n = 179$ ) or bipolar disorder ( $n = 105$ ) and population-based controls (PBC,  $n = 181$ ). Children and parents were assessed with The Social Responsiveness Scale, Second Edition. Duration of time each parent and child have lived together was ascertained through interviews. Parents with schizophrenia and parents with bipolar disorder exhibited poorer social responsiveness compared with PBC parents. Parents with schizophrenia displayed poorer social responsiveness compared with parents with bipolar disorder. Schizophrenia co-parents exhibited poorer social responsiveness compared with bipolar co-parents and PBC co-parents. We found significant positive associations between parents' and children's social responsiveness, with no interaction effect of duration of time living together. Considering that social impairments are suggested as a vulnerability marker, this knowledge calls for increased attention towards vulnerable families, particularly those where both parents have social impairments.

### 1. Introduction

Schizophrenia and bipolar disorder are severe mental disorders associated with social impairments such as social cognitive deficits and poor social functioning (Burns and Patrick, 2007; Gillissie et al., 2022; Green et al., 2015; Samamé, 2013; Savla et al., 2013). A large body of research has focused on identifying those social domains mostly affected in schizophrenia and bipolar disorder. Social impairments can be

categorized into three multidimensional constructs (social cognition, social skills, and social functioning), nested within each other. Social cognition can be defined as the narrowest construct underlying the wider construct of social skills that again contributes to the broadest construct of social functioning (Vangkilde et al., 2016; Yager and Ehmann, 2006). Research in schizophrenia and bipolar disorder has mostly focused on social cognition and social functioning. However, prior studies of social skills have demonstrated poorer social

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competence, social appropriateness, and social knowledge both in schizophrenia (Depp et al., 2010; Miller et al., 2021; Patterson et al., 2001; Sitzer et al., 2008) and bipolar disorder (Goldstein et al., 2006; Miller et al., 2021). It can be argued that social responsiveness is another measure of social skills as it refers to the ability to understand and engage in social interactions with other people in an appropriate way. Specifically, it involves processing social information, comprehending the message being conveyed, responding appropriately, and being motivated to engage in interpersonal interactions (Constantino et al., 2000). To our knowledge, only a single study has investigated social responsiveness in adults with schizophrenia or bipolar disorder and the results imply that both remitted and non-remitted patients have poorer social responsiveness compared with controls (Matsuo et al., 2015).

Children typically resemble their parents, not only physically but also in terms of their social behavior, skills, and/or appearance. This resemblance presumably occurs due to a combination of genetic and environmental factors (Plomin and Daniels, 2011; Rice, 2008). Results from our previous study showed that children at familial high-risk of schizophrenia (FHR-SZ), and to some extent also children at familial high-risk of bipolar disorder (FHR-BP), exhibit poorer social responsiveness compared to population-based controls (PBC) both at age 7 and at age 11 (Christiani et al., 2019; Veddum et al., 2022). However, it remains unknown whether these children's social responsiveness reflects their parents' social responsiveness, but previous studies of the general population found strong associations between parental and offspring social responsiveness (Constantino and Todd, 2005; Lyall et al., 2014). In the light of the fact that parents with schizophrenia or bipolar disorder are likely to exhibit social impairments (Burns and Patrick, 2007; Gillissie et al., 2022; Green et al., 2015; Samamé, 2013; Savla et al., 2013), and that their offspring are at increased risk of developing a mental disorder themselves (Rasic et al., 2013), similar studies in high-risk populations are indeed relevant as social impairments have been suggested as a potential vulnerability marker both disorders (Bora and Pantelis, 2013; Bora and Özerdem, 2017; Lavoie et al., 2013). Additionally, partners to individuals with a mental disorder have a higher prevalence of psychiatric illness compared with the general population (Greve et al., 2021; Merikangas and Spiker, 1982; Nordsletten et al., 2016), and may thereby also be more likely to display social impairments. A few studies of the general population found moderate positive correlations between parents' social responsiveness (Constantino and Todd, 2005; Lyall et al., 2014). However, this remains uninvestigated in samples where one parent is diagnosed with a severe mental disorder even though that it may have implications for the familial transmission of social impairments. Besides, investigation of the association between parents' and children's social responsiveness in families with parental schizophrenia or bipolar disorder may help to shed light on social impairments as a potential liability marker and eventually facilitate identification of particularly vulnerable children.

Thereby, the aim of the present paper was twofold. We aimed to 1) examine social responsiveness in parents with schizophrenia or bipolar disorder and their co-parents, and 2) investigate the association of social responsiveness between parents' and their 11-year-old offspring, and further to study the effect of duration of time parent and child have lived together.

## 2. Materials and methods

This study is a part of the first follow-up of The Danish High Risk and Resilience Study – VIA, which is a longitudinal familial high-risk study of children born to parents with schizophrenia or bipolar disorder and PBC (Thorup et al., 2018, 2015). Data collection for the baseline study was carried out between January 1st, 2013 and January 1st, 2016, whereas data collection for the first follow-up took place from March 1st, 2017, to June 30th, 2020. Data was collected and stored using Research Electronic Data Capture tools (Harris et al., 2019, 2009). The Danish High Risk and Resilience Study was carried out in accordance

with The Code of Ethics of the World Medical Association and was approved by the Danish Data Protection Agency (dispensation from 1st of March 2017) and The National Committee on Health Research Ethics (ref. H16043682).

### 2.1. Participants

Initially, the cohort consisted of 522 7-year-old children and their biological parents of whom at least one parent was diagnosed with schizophrenia ( $n = 202$ ), bipolar disorder ( $n = 120$ ), or none of these disorders (i.e., PBC,  $n = 200$ ). Participants were identified through Danish Registers (Mors et al., 2011; Pedersen et al., 2006). The PBC children were matched one-to-one to the FHR-SZ children based on age, sex, and municipality. The FHR-BP children were a non-matched sample but did not differ from the two other groups in terms of sex and age. At four-year follow-up, a total of 465 families participated (FHR-SZ,  $n = 179$ ; FHR-BP,  $n = 105$ ; PBC,  $n = 181$ ), corresponding to a retention rate of 89%. All participants received written and verbal information about the study and written informed consent was obtained from the legal guardians of the participating children and from the participating adults themselves.

The index parent was defined as the parent registered with a diagnosis of schizophrenia or bipolar disorder. Contrary, the co-parent was defined as the other parent without schizophrenia or bipolar disorder. PBC parents and co-parents could have any other mental disorder than schizophrenia and bipolar disorder. The sex of the schizophrenia index parent and the schizophrenia co-parent defined the sex of the index PBC parent and the PBC co-parent in the matched family.

### 2.2. Measurements

We assessed social responsiveness with the Social Responsiveness Scale, Second Edition (SRS-2), which is a well-validated 65-item rating scale designed to identify the presence and severity of social impairments associated with autism spectrum disorders (Constantino and Gruber, 2012). However, the questionnaire has also been widely administered in non-autistic samples, as it is also relevant when identifying the behavior of individuals whose social deficits falls below the threshold for a diagnosis of autism, but who nonetheless may need support (Constantino, 2011; Constantino et al., 2000). Parents completed the SRS-2 Adult Self-report Form, and the SRS-2 School-Age Form was completed by the teacher who knew the child best in school settings. SRS-2 provides a global score ranging from 0 (highly socially competent) to 195 (severely socially impaired). The scale can be divided into two well-validated and highly correlated subscales; Social Communication and Interaction (SCI) and Restricted Interests and Repetitive Behavior (RIRB) (Frazier et al., 2014). Here, we included the subscales in order to be able to distinguish between items related to social responsiveness (SCI) and highly autistic-like items (RIRB), as we were particularly interested in the SCI subscale.

Duration of time each parent had lived with the child was assessed through interviews. Both parents were asked to clarify for how many months they had lived with their child from one year before birth until age 11. In cases where the parents did not live together, the parent living most of the time with the child was noted as living with the child full time, whereas the other parent was noted as not living with the child. In half-and-half cases, both parents were noted as living with the child half of the time.

### 2.3. Statistical analyses

One-way ANOVA or chi-square tests were used in analyses of descriptive and clinical characteristics, followed by pairwise comparisons, when relevant. A categorical variable with three categories for duration of time parent and child had lived together was constructed: 1) half of the time or less, 2) more than half of the time, and 3) all the time.

As advised in the manual, missing items on SRS-2 were assigned with the particular item's median score with a maximum of six missing answers for each respondent (Constantino and Gruber, 2012). Between-group differences on children's and parents' SRS-2 scores were examined using linear regression analyses with the SRS-2 outcome as the dependent variable and familial high-risk (FHR) status as the independent variable. Cluster robust variance estimation was used to account for clustering at family level for the comparison of children's social responsiveness.

The association between index parents' and co-parents' SRS-2 scores was ascertained using linear regression analyses with the co-parent's SRS-2 outcome as the dependent variable and the co-parent's SRS-2 outcome as the independent variable. Families where both parents were diagnosed with schizophrenia or bipolar disorder were excluded from these analyses. Likewise, the association between index parents' or co-parents' and children's SRS-2 scores was ascertained using linear regression analyses with the child's SRS-2 outcome as the dependent variable and the parent's SRS-2 outcome as the independent variable. Using multiple linear regression analyses, we examined the interaction effect of FHR status on all associations. In the event of a non-significant interaction, the interaction term was removed, and the models were subsequently adjusted for FHR status. Additionally, we examined the interaction effect of duration of time living together. Cluster robust variance estimation was used to account for clustering at family level. To compare index parents', co-parents', and children's SRS-2 scores based on duration of time parent and child had lived together, we used linear regression analyses with the SRS-2 outcome as the independent variable and duration of time living together as the independent variable.

Effect sizes were calculated using Cohen's *d* (small, 0.2; medium, 0.5; and large, 0.7) (Cohen, 1988). Alpha level was set to 0.05 for all statistical analyses. When relevant, the false discovery rate in the multiple comparisons were calculated according to the Benjamini-Hochberg correction procedure with the *q*-value set to 0.05 (Benjamini and Hochberg, 1995). All analyses were conducted using Stata IC software, version 16.1 (StataCorp., 2019).

### 3. Results

#### 3.1. Sample characteristics

Data was available from 336 index parents (FHR-SZ, *n* = 113; FHR-BP, *n* = 80; PBC, *n* = 143), 297 non-index parents (FHR-SZ, *n* = 116; FHR-BP, *n* = 65; PBC, *n* = 116), and 392 children (FHR-SZ, *n* = 147; FHR-BP, *n* = 89; PBC, *n* = 156).

More schizophrenia index parents were females compared with bipolar index parents. Schizophrenia index parents were younger than bipolar index parents and PBC index parents. Similarly, schizophrenia co-parents were younger than bipolar co-parents and PBC co-parents. Schizophrenia index parents and bipolar index parents had lived less time with their child compared with PBC index parents (see Table 1).

#### 3.2. Comparisons of parents' social responsiveness

Schizophrenia index parents and bipolar index parents exhibited poorer social responsiveness compared with PBC index parents, with medium to large effect sizes (ranging from 0.66 to 0.90). Schizophrenia co-parents displayed poorer social responsiveness compared with PBC co-parents and bipolar co-parents (only the SRS-2 global score and the SCI subscale score), with medium effect sizes (ranging from 0.33 to 0.37) (see Fig. 1a-b and Table S1).

We observed no significant interaction effects of FHR status on the association between index parents' and co-parents' social responsiveness (see Table S2). Additionally, we found no significant associations between index parents' and co-parents' SRS-2 scores, neither in unadjusted analyses nor in analyses adjusted for FHR status (see Table 2).

#### 3.3. Associations between parents' and children's social responsiveness

We observed no significant interaction effects of FHR status neither on the associations between index parents and children nor between co-parents and children (see Table S3).

We found significant positive associations both between index parents' and children's social responsiveness as well as between co-parents'

**Table 1**  
Demographic and clinical characteristics of the participating parents and their 11-year-old children.

	FHR-SZ	FHR-BP	PBC	p-value	Pairwise comparisons		
					FHR-SZ vs PBC	FHR-BP vs PBC p-value	FHR-SZ vs FHR-BP
<b>Index parents<sup>a</sup>, N</b>	113	80	143				
Female, N (%)	86 (76.11)	45 (56.25)	99 (69.23)	<b>0.013<sup>C</sup></b>	0.222	0.052	<b>0.004</b>
Age at inclusion, mean (SD)	41.60 (6.07)	44.88 (6.45)	44.60 (4.71)	<b>&lt;0.001<sup>A</sup></b>	<b>&lt;0.001</b>	0.721	<b>&lt;0.001</b>
Lived with child from age 0–11 <sup>c</sup> , N (%):							
Half of the time or less	16 (15.53)	12 (16.00)	6 (4.32)	<b>&lt;0.001<sup>C</sup></b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.986
More than half of the time	28 (27.18)	21 (28.00)	10 (7.19)				
All the time	59 (57.28)	42 (56.00)	123 (88.49)				
<b>Co-parents<sup>b</sup>, N</b>	116	65	116				
Female, N (%)	63 (54.31)	40 (61.54)	66 (56.90)	0.642 <sup>C</sup>	–	–	–
Age at inclusion, mean (SD)	43.32 (6.32)	45.68 (5.81)	44.76 (4.19)	<b>0.015<sup>A</sup></b>	<b>0.046</b>	0.277	<b>0.006</b>
Lived with child from age 0–11 <sup>d</sup> , N (%):							
Half of the time or less	11 (10.28)	1 (1.61)	6 (5.31)	0.117 <sup>C</sup>	–	–	–
More than half of the time	22 (20.56)	12 (19.35)	16 (14.16)				
All the time	74 (69.16)	49 (79.03)	91 (80.53)				
<b>Children, N</b>	147	89	156				
Female, N (%)	67 (45.58)	41 (46.07)	72 (46.15)	0.994 <sup>C</sup>	–	–	–
Age at inclusion, mean (SD)	11.95 (0.27)	11.95 (0.21)	11.93 (0.22)	0.574 <sup>A</sup>	–	–	–

Abbreviations: Familial high-risk of schizophrenia (FHR-SZ); Familial high-risk of bipolar disorder (FHR-BP); Population-based controls (PBC).

<sup>a</sup> Index parent refers to the biological parent registered with a diagnosis of schizophrenia or bipolar disorder. The sex of the schizophrenia index parent defined the sex of the PBC index parent in the matched family.

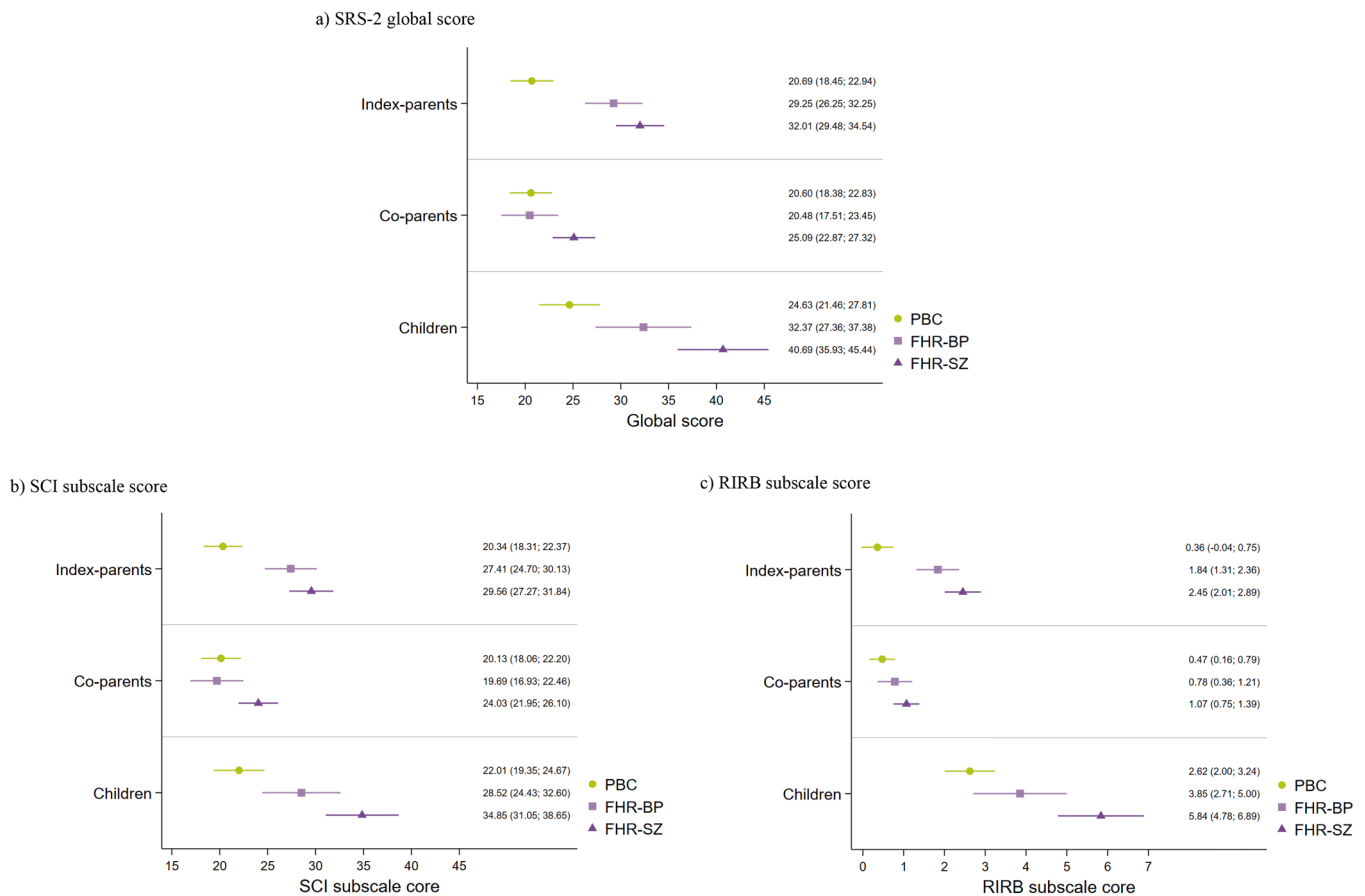
<sup>b</sup> The co-parent is the biological parent not registered with schizophrenia or bipolar disorder. The sex of the schizophrenia co-parent defined the sex of the PBC co-parent in the matched family.

<sup>c</sup> Based on data from 317 index parents (SZ, *n* = 103; BP, *n* = 75; PBC, *n* = 139).

<sup>d</sup> Based on data from 282 non-index parents (FHR-SZ, *n* = 107; FHR-BP, *n* = 62; PBC, *n* = 113).

<sup>A</sup> One-way ANOVA, significance level *p* < 0.05.

<sup>C</sup> Chi-square test, significance level *p* < 0.05.



**Fig. 1.** Index parents', co-parents', and children's scores on the Social Responsiveness Scale, Second Edition (SRS-2). Abbreviations: Familial high-risk of schizophrenia (FHR-SZ), Familial high-risk of bipolar disorder (FHR-BP), Populations-based controls (PBC), Social Communication and Interaction (SCI), Restricted Interests and Repetitive Behavior (RIRB). Note: Index parent refers to the biological parent registered with a diagnosis of schizophrenia or bipolar disorder. The co-parent is the biological parent not registered with a diagnosis of schizophrenia or bipolar disorder. The sex of the schizophrenia index parent and the schizophrenia co-parent defined the sex of the PBC index parent and the PBC co-parent in the matched family. Note: Child data has already been presented elsewhere (Veddum et al., 2022). Due to methodological differences, minor divergencies exist between the previous published results and the results presented here.

**Table 2**  
Associations between index parents' and co-parents' social responsiveness.

	Unadjusted model			Adjusted model*		
	Coefficient	95% CI	p-value	Coefficient	95% CI	p-value
SRS-2 Global Score	0.06	-0.06-0.17	0.317	0.02	-0.11-0.14	0.781
Social Communication and Interaction (SCI)	0.05	-0.07-0.17	0.392	0.02	-0.11-0.15	0.763
Restricted Interests and Repetitive Behavior (RIRB)	0.02	-0.08-0.11	0.735	-0.04	-0.14-0.06	0.421

Abbreviations: The Social Responsiveness Scale, Second Edition (SRS-2), p-value = significance level  $p < 0.05$ . Note: Index parent refers to the biological parent registered with a diagnosis of schizophrenia or bipolar disorder, and the co-parent is the biological not diagnosed with schizophrenia or bipolar disorder. The sex of the schizophrenia index parent and the schizophrenia co-parent defined the sex of the population-based control index parent and the population-based control co-parent in the matched family. These analyses involved 192 parent pairs (FHR-SZ,  $n = 66$ ; FHR-BP,  $n = 46$ ; PBC,  $n = 80$ ). \* Model adjusted for familial high-risk status.

and children's social responsiveness, signifying that higher parental scores on SRS-2 were associated with higher scores for children. This was evident both for unadjusted analyses and analyses adjusted for FHR status on all SRS-2 outcomes (see Table 3). We found no significant interaction effect of duration of time living together on the association between index parents' and children's social responsiveness (SRS-2 global score,  $F(2, 267) = 1.01, p = 0.365$ ; SCI,  $F(2, 267) = 0.94, p = 0.392$ ; RIRB,  $F(2, 267) = 1.80, p = 0.168$ ) (see

Figure S1a-c). Likewise, we found no significant interaction effect of duration of time living together on the association between co-parents' and children's social responsiveness (SRS-2 global score,  $F(2, 248) = 2.39, p = 0.093$ ; SCI,  $F(2, 248) = 2.99, p = 0.052$ , RIRB,  $F(2, 248) = 0.87, p = 0.419$ ) (see Figure S2a-c).

**Table 3**  
Associations between parents' and children's social responsiveness.

	Unadjusted model			Adjusted model*		
	Coefficient	95% CI	p-value	Coefficient	95% CI	p-value
<b>Index parent<sup>a</sup></b>						
SRS-2 Global Score	0.55	0.31–0.77	<0.001	0.42	0.18–0.65	0.001
Social Communication and Interaction (SCI)	0.48	0.28–0.68	<0.001	0.37	0.18–0.58	<0.001
Restricted Interests and Repetitive Behavior (RIRB)	0.50	0.18–0.81	0.002	0.32	0.02–0.63	0.039
<b>Co-parent<sup>b</sup></b>						
SRS-2 Global Score	0.56	0.28–0.85	<0.001	0.48	0.18–0.77	0.002
Social Communication and Interaction (SCI)	0.46	0.22–0.70	<0.001	0.39	0.14–0.64	0.002
Restricted Interests and Repetitive Behavior (RIRB)	1.05	0.66–1.43	<0.001	0.95	0.56–1.35	<0.001

Abbreviations: The Social Responsiveness Scale, Second Edition (SRS-2), p-value = significance level  $p < 0.05$ .

<sup>a</sup> Index parent refers to the biological parent with a registered with schizophrenia or bipolar disorder. The sex of the index schizophrenia parent defined the sex of the population-based control parent in the matched family. These analyses involved 279 index parents (FHR-SZ,  $n = 91$ ; FHR-BP,  $n = 66$ ; PBC,  $n = 122$ ).

<sup>b</sup> The co-parent is the biological parent not diagnosed with schizophrenia or bipolar disorder. The sex of the schizophrenia co-parent defined the sex of the population-based control co-parent in the matched family. These analyses involved 260 non-index parents (FHR-SZ,  $n = 101$ ; FHR-BP,  $n = 57$ ; PBC,  $n = 102$ ).

\* Model adjusted for familial high-risk status.

### 3.4. Social responsiveness based on duration of time living together

We observed significant differences between index parents' social responsiveness dependent on duration of time lived with their child, primarily with medium to large effect sizes. Specifically, index parents who had lived with their child half the time or less exhibited poorer social responsiveness both compared with index parents who had lived with their child more than half of the time or all the time. Similarly, index parents who had lived with their child more than half of the time displayed poorer social responsiveness compared with index parents who had lived with their child all the time. Likewise, the children's

social responsiveness varied according to duration of time living together with the index parent, with medium to large effect sizes. Children who had lived with the index parent half of the time or less as well as children who had lived with the index parent more than half of the time exhibited poorer social responsiveness compared with children who had lived with the index parent all the time. Similarly, children who had lived with the co-parent half of the time or less displayed poorer social responsiveness compared with children who had lived with the co-parent all the time, with medium effect sizes (see Table 4).

**Table 4**  
Pairwise comparisons on results from the social responsiveness scale, second edition, based on duration of time parent and child have lived together.

	Half of the time or less (1) Mean (95% CI)	More than half of the time (2)	All the time (3)	Pairwise comparisons		
				1 vs. 2 p-value (d)	1 vs. 3	2 vs. 3
<b>Index parent<sup>a</sup>, N</b>						
	34	59	224			
SRS-2 Global score	37.79 (33.32–42.26)	28.90 (25.50–32.29)	23.31 (21.57–25.05)	0.002 (0.59)	<0.001 (1.11)	0.004 (0.44)
Social Communication and Interaction (SCI)	22.50 (20.92–24.08)	27.03 (23.95–30.12)	34.32 (30.26–38.39)	0.005 (0.55)	<0.001 (0.99)	0.011 (0.36)
Restricted Interests and Repetitive Behavior (RIRB)	0.81 (0.51–1.11)	1.86 (1.28–2.45)	3.47 (2.70–4.24)	0.001 (0.49)	<0.001 (1.24)	0.002 (0.52)
<b>Children living with index, N</b>						
	38	57	232			
SRS-2 Global score	42.21 (32.35–52.07)	40.65 (32.82–48.48)	27.04 (24.38–29.70)	0.807 (0.05)	0.004 (0.68)	0.001 (0.60)
Social Communication and Interaction (SCI)	36.13 (28.15–44.11)	34.61 (28.43–40.80)	24.14 (21.92–26.36)	0.767 (0.06)	0.005 (0.64)	0.002 (0.56)
Restricted Interests and Repetitive Behavior (RIRB)	3.34 (2.07–4.62)	2.02 (1.25–2.79)	0.85 (0.60–1.10)	0.079 (0.40)	<0.001 (1.14)	0.005 (0.56)
<b>Co-parent<sup>b</sup>, N</b>						
	18	50	214			
SRS-2 Global score	23.94 (18.26–29.63)	24.24 (20.83–27.65)	21.76 (20.11–23.41)	0.930 (0.02)	0.468 (0.18)	0.198 (0.20)
Social Communication and Interaction (SCI)	23.33 (18.04–28.64)	23.16 (19.98–26.34)	21.06 (19.52–22.59)	0.956 (0.01)	0.417 (0.20)	0.242 (0.18)
Restricted Interests and Repetitive Behavior (RIRB)	0.61 (0.12–1.11)	1.04 (0.60–1.48)	0.70 (0.46–0.94)	0.331 (0.31)	0.835 (0.05)	0.170 (0.21)
<b>Children living with the co-parent, N</b>						
	16	55	254			
SRS-2 Global score	38.75 (25.21–52.29)	41.38 (33.27–49.49)	27.67 (25.01–30.32)	0.743 (0.09)	0.115 (0.51)	0.002 (0.59)
Social Communication and Interaction (SCI)	32.94 (22.10–43.78)	34.84 (28.64–41.03)	24.63 (22.40–26.85)	0.765 (0.08)	0.140 (0.45)	0.003 (0.54)
Restricted Interests and Repetitive Behavior (RIRB)	0.61 (–0.20–1.42)	1.08 (0.59–1.57)	0.70 (0.47–0.94)	0.205 (0.28)	0.759 (0.05)	0.182 (0.19)

Abbreviations: Social Responsiveness Scale, Second Edition (SRS-2); Confidence Intervals (CI);  $d$  = Cohens  $d$ ; p-value = significance level  $p < 0.05$ ; After correction according to the Benjamini-Hochberg procedure for the SRS-2 outcomes,  $p < 0.05$  for index parents,  $p < 0.033$  for children living with index, and  $p < 0.011$  for children living with non-index.

<sup>a</sup> Index parent refers to the biological parent registered with a diagnosis of schizophrenia or bipolar disorder. The sex of the schizophrenia index parent defined the sex of the population-based control index parent in the matched family.

<sup>b</sup> The co-parent is the biological parent not diagnosed with schizophrenia or bipolar disorder. The sex of the schizophrenia co-parent defined the sex of the population-based control co-parent in the matched family.

#### 4. Discussion

In this representative and population-based cohort study, we aimed to investigate social responsiveness in families with parental schizophrenia or bipolar disorder. Parents with schizophrenia or bipolar disorder displayed poorer social responsiveness compared with PBC parents. Likewise, schizophrenia co-parents exhibited poorer social responsiveness compared with bipolar co-parents and PBC co-parents. Irrespectively of FHR status, we found positive associations between parents' and children's social responsiveness, which was not significantly affected by duration of time parent and child had lived together.

In accordance with our expectations, parents with schizophrenia or bipolar disorder exhibited poorer social responsiveness compared with PBC parents. This finding is in line with a previous study of remitted and non-remitted outpatients (Matsuo et al., 2015) as well as prior studies demonstrating poorer social skills both in schizophrenia (Depp et al., 2010; Miller et al., 2021; Patterson et al., 2001; Sitzler et al., 2008) and bipolar disorder (Goldstein et al., 2006; Miller et al., 2021). Further, our results revealed that the index parents' social responsiveness were poorer for those who had lived least with their child, presumably representing a subgroup of parents who are more severely affected by disorder-related factors. Social dysfunction is related to symptom severity and thereby is less severe in remitted and high-functioning individuals with schizophrenia (Bora et al., 2008; Brissos et al., 2011; Jaracz et al., 2015; Sprong et al., 2007). Nevertheless, our findings are in agreement with previous evidence that both disorders are associated with social impairments such as social cognitive deficits and poor social functioning (Burns and Patrick, 2007; Gillissie et al., 2022; Green et al., 2015; Samamé, 2013; Savla et al., 2013). However, in addition to social cognitive deficits and poor social functioning, our results emphasize that social impairment also involves poorer social skills.

We established no significant associations between index parents' and co-parents' social responsiveness, which is incongruent with previous studies of the general population (Constantino and Todd, 2005; Lyall et al., 2014). Importantly though, schizophrenia co-parents exhibited poorer social responsiveness both compared with bipolar co-parents and PBC co-parents. This indicates that children in families with parental schizophrenia have a higher risk of growing up with two parents with social impairments, whereas children in families with parental bipolar disorder presumably have at least one parent with well-functioning social responsiveness comparable to that of PBC parents. In addition, we found significant positive associations between index parents' and children's social responsiveness as well as between co-parents' and children's social responsiveness, irrespectively of FHR status. This finding is in line with previous studies of the general population (Constantino and Todd, 2005; Lyall et al., 2014). Notably, social impairments have been suggested as a vulnerability marker especially for schizophrenia (Bora and Pantelis, 2013; Lavoie et al., 2013), but also bipolar disorder (Bora and Özerdem, 2017). Thereby, this knowledge should be taken into consideration when designing identification strategies of particularly vulnerable children with elevated need of social support.

As expected, we found that both parents with schizophrenia and parents with bipolar disorder had lived less with their child compared to PBC parents, presumably due to illness related factors such as hospitalization and poor functioning. In families with parental schizophrenia or bipolar disorder, this may very well affect the degree to which the children have been exposed to their index parents' poor social responsiveness as we found that the index parents who had lived least with their children displayed poorer social responsiveness. However, our results further revealed that children who had lived least with the index parent exhibited poorer social responsiveness, indicating that the most severely affected parents have the most affected children. Moreover, this is in accordance with the identified positive association between index parents' and children's social responsiveness. We showed no differences in how much co-parents had lived with their child indicating that

children in families with parental schizophrenia are most likely exposed to the poorer social responsiveness of the co-parent without schizophrenia or bipolar disorder.

Surprisingly, we observed no significant interaction effects of duration of time living together on the association between parents' and children's social responsiveness. A possible explanation relates to the composition of the variable as it can be argued that it is merely a rough estimate of how much the parent and child have lived together rather than a detailed assessment. Moreover, living together does not necessarily reflect the quality of or actual time spend together, and other environmental factors may also impact the association between parents' and children's social responsiveness. Nevertheless, the parents may in themselves constitute a risk factor, not only due to the genetic liability, but also due to their significant contribution to the child's environment (Uher and Zwicker, 2017). Future studies should aim at further investigating the interaction between genetic and environmental factors influencing the intergenerational transmission of social impairments in families with parental schizophrenia or bipolar disorder.

The current study has several strengths including the large sample size, assessment of multiple FHR groups, and appliance of a validated measure, which for the children were completed by a teacher (and not the parents under examination). Moreover, it is the first FHR study to link data on social responsiveness from parents and children, of whom all children had the same age diminishing possible effects of age-related differences. Our population-based cohort is highly unique as participants were extracted from the registers, which enhances representativity. However, a noteworthy limitation is that the information on duration of time living together was merely based on a rough estimate rather than an exact assessment of the actual time spent together. Moreover, this information required participation both at baseline and follow-up. Nevertheless, this is the first FHR study attempting to assess real life exposure to parental mental illness by assessing duration of time parent and child had lived together.

In conclusion, this study is the first to investigate social responsiveness in families with parental schizophrenia or bipolar disorder compared with PBC. Offspring of parents with schizophrenia or bipolar disorder are more likely to be exposed to poor social responsiveness. However, this appears to be more pronounced in families with parental schizophrenia where both parents display poorer social responsiveness. The familial transmission of social responsiveness presumably occurs due to both genetic and environmental factors. In general, more research in this field is warranted, and future studies should aim at applying various measures capturing different aspects of social impairment.

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#### CRediT authorship contribution statement

**Lotte Veddem:** Conceptualization, Methodology, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing. **Maja Gregersen:** Investigation, Writing – review & editing. **Anna Krogh Andreassen:** Investigation, Writing – review & editing. **Christina Bruun Knudsen:** Investigation, Writing – review & editing. **Julie Marie Brandt:** Investigation, Writing – review & editing. **Mette Falkenberg Krantz:** Investigation, Writing – review & editing. **Anne**

**Søndergaard:** Investigation, Writing – review & editing. **Birgitte Klee Burton:** Writing – review & editing. **Jens Richardt Møllegaard Jepsen:** Writing – review & editing. **Nicoline Hemager:** Project administration, Writing – review & editing. **Anne Amalie Elgaard Thorup:** Project administration, Writing – review & editing. **Merete Nordentoft:** Funding acquisition, Project administration, Writing – review & editing. **Ole Mors:** Funding acquisition, Project administration, Writing – review & editing. **Vibeke Bliksted:** Project administration, Writing – review & editing. **Aja Neergaard Greve:** Conceptualization, Methodology, Project administration, Writing – review & editing.

## Declaration of Competing Interest

All contributing authors declare no conflicts of interest.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.psychres.2023.115140](https://doi.org/10.1016/j.psychres.2023.115140).

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