Psychiatry Research 321 (2023) 115092

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Affective lability in parents with schizophrenia or bipolar disorder and their co-parents - The Danish High Risk and Resilience Study VIA 7

Nanna Lawaetz Steffensen [a,b], Nicoline Hemager [b,c,d], Anette Faurskov Bundgaard [a,b], Ditte Lou Gantriis [a,b], Birgitte Klee Burton [b,d,e,f], Ditte Ellersgaard [b,c], Anders Helles Carlsen [g], Vibeke Bliksted [a,b,h], Kerstin J. Plessen [b,d,i], Jens Richardt Møllegaard Jepsen [b,c,d,j], Merete Nordentoft [b,c], Anne A.E. Thorup [b,d,e], Ole Mors [a,b], Aja Neergaard Greve [a,b,h,*]

[a] Psychosis Research Unit, Aarhus University Hospital, Psychiatry, Denmark
[b] The Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH), Aarhus, Denmark
[c] Copenhagen Research Centre for Mental Health (CORE), Mental Health Centre Copenhagen, Copenhagen University Hospital, Kildegaardsvej 28, building 15, 4th, Hellerup 2900, Denmark
[d] Child and Adolescent Mental Health Centre, Mental Health Services Capital Region, Research Unit, Copenhagen University Hospital, Gentofte, Hospitalsvej 3A, 1st floor, Hellerup 2900, Denmark
[e] Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamsvej 3B, Copenhagen N 2200, Denmark
[f] Department of Child and Adolescent Psychiatry, Copenhagen University Hospital – Psychiatry Region Zealand, Roskilde, Denmark
[g] Aarhus University Hospital, Psychiatry, Denmark
[h] Department of Clinical Medicine, Faculty of Health, Aarhus University, Palle Juul-Jensens Boulevard 82, Aarhus N 8200, Denmark
[i] Division of Child and Adolescent Psychiatry, Department of Psychiatry, University Hospital Lausanne and University of Lausanne, Switzerland
[j] Centre for Neuropsychiatric Schizophrenia Research & Centre for Clinical Intervention and Neuropsychiatric Schizophrenia Research, Mental Health Centre Glostrup, Copenhagen University Hospital, Ndr. Ringvej 29-67, Glostrup 2600, Denmark

ARTICLE INFO

Keywords:
Mental disorders
Assortative mating
Nonrandom mating
Parents
Schizophrenia
Bipolar disorder

ABSTRACT

In bipolar disorder, dysregulation of affect is a core feature while knowledge on affective lability in schizophrenia is sparse. Research on affective lability in partners to individuals with schizophrenia or bipolar disorder is also lacking. The objective of this study was to investigate affective lability in parents with schizophrenia or bipolar disorder, and their co-parents without these disorders. The Danish High Risk and Resilience Study – VIA 7 is a population-based cohort study. This study focuses on parents diagnosed with schizophrenia ($n = 148$), their co-parents ($n = 157$), parents with bipolar disorder ($n = 98$), their co-parents ($n = 89$) and control parents ($n = 359$). The Affective Lability Scale – short form (ALS-SF) was used to measure affective lability. We found significantly higher levels of affective lability in parents with schizophrenia and bipolar disorder compared with controls, but no significant differences between bipolar disorder and schizophrenia. Co-parents to parents with schizophrenia had significantly higher levels of affective lability compared to controls. Our results add to the existing knowledge concerning underlying transdiagnostic factors and nonrandom mating in schizophrenia and bipolar disorder and highlight the need for studies of parental affective lability as a potential risk factor for offspring in families with parental schizophrenia or bipolar disorder.

1. Introduction

Affective instability can be defined as rapid oscillations of intense affect with difficulty regulating these oscillations or their behavioral consequences (Marwaha et al., 2014). Studies have demonstrated associations between affective instability and various mental disorders with elevated affective instability being linked to a more complex and severe illness course and outcome (Høegh et al., 2020). The term affective instability has been conceptualized into three core components concerning the intensity of affective responsiveness, the ability to control affective states, and affective lability (Larsen et al., 1987). Affective lability refers to the propensity to experience excessive and unpredictable changes in affective states (Zwicker et al., 2019). Of the three components, affective lability is most commonly investigated and

* Corresponding author at: Psychosis Research Unit, Aarhus University Hospital Psychiatry, Palle Juul-Jensens Blv. 175, Aarhus N DK-8200, Denmark.
E-mail address: ajagreve@rm.dk (A.N. Greve).

https://doi.org/10.1016/j.psychres.2023.115092
Received 16 December 2022; Received in revised form 31 January 2023; Accepted 2 February 2023
Available online 5 February 2023

appears to have the highest impact on the level of function (Marwaha et al., 2018). Studies have found higher levels of affective lability across a wide range of different mental disorders as well as in first-degree relatives of individuals with bipolar disorder (Marwaha et al., 2018; Aas et al., 2015).

Schizophrenia and bipolar disorder are severe mental disorders that typically develop in adolescence or young adulthood and often cause lifelong disabilities (Murray et al., 2004). In bipolar disorder, dysregulation of affect is a core feature and elevated affective lability is strongly associated with the disorder (Høegh et al., 2020). Affective lability has been documented in periods of euthymia (Henry et al., 2008), and in all polarities of the illness episodes in bipolar disorder (Henry et al., 2003). Affective lability is present early in the course of the illness (Aminoff et al., 2012) and appears to be a both trait- and state-dependent factor associated with poor prognostic outcomes (Høegh et al., 2020; Henry et al., 2008; O'Donnell et al., 2018). Poor affect regulation has been suggested as an underlying mechanism across several mental disorders and thereby a transdiagnostic construct. To our knowledge, only a few studies have examined affective lability in individuals with schizophrenia (Høegh et al., 2020; Høegh et al., 2021), and they indicate that affective lability is markedly elevated in individuals with schizophrenia and bipolar disorder with equally high elevations in both groups compared with healthy controls (Høegh et al., 2020; Høegh et al., 2021). However, more research is needed to confirm or reject this association.

Nonrandom mating refers to a tendency for mated couples to be more similar regarding some phenotypic traits than would be the case if mating occurred completely at random. Nonrandom mating is common in individuals with mental disorders, both within specific disorders and across the spectrum of mental disorders (Merikangas and Spiker, 1982; Nordsletten et al., 2016). We recently reported evidence for nonrandom mating for psychiatric disorders, social functioning, and processing speed as well as for genetic assortative mating in the Danish High Risk and Resilience Study (Greve et al., 2021; Jefsen et al., 2022). Here we found that co-parents to parents with schizophrenia or bipolar disorder more often fulfilled the criteria for a mental disorder and had poorer social functioning compared to parents from the control group. And furthermore, co-parents to parents with schizophrenia performed poorer on processing speed compared to parents from the control group. To our knowledge, no studies exist on affective lability in partners to individuals diagnosed with schizophrenia or bipolar disorder which is of special importance in the context of child-rearing. It is reasonable to assume that high levels of affective lability are related to difficulties with parental role functioning and that elevated levels of affective lability in parents thus may affect parenting, the emotional atmosphere in the home, and thus child development (Lunkenheimer et al., 2007; Cohler and Musick, 1983). If a parent is ill, the care for the child will often – at least in periods - depend on the co-parent. Thus, elevated affective lability in parents and co-parents may be a potential risk factor for the children in these families in addition to the effects of the genetic risk.

Therefore, we aim to compare affective lability in five groups of parents:

- Parents with schizophrenia (SZ).
- Parents with bipolar disorder (BP).
- Co-parents to parents with schizophrenia (SZ-co).
- Co-parents to parents with bipolar disorder and (BP-co).
- Parents from a control group (PBC).

We hypothesized that parents with SZ and parents with BP will present with higher levels of affective lability compared to PBC and that SZ-co and BP-co will show more affective lability than PBC.

2. Methods

The Danish High Risk and Resilience Study – VIA 7 is a population-based cohort study conducted in Denmark from 1 January 2013 until 31 January 2016. The VIA 7 sample consists of 522 7-year-old children with no parent, one parent, or both parents diagnosed with schizophrenia or bipolar disorder. The design of VIA 7 has been described in detail elsewhere (Thorup et al., 2015). This study focused on the parents from the VIA 7 cohort.

2.1. Participants

Participants were identified in the Danish Civil Registration System (Pedersen et al., 2006) and the Danish Psychiatric Central Research Register (Mors et al., 2011) through linkage of the unique personal identification number assigned to all Danish citizens. The Danish Psychiatric Central Research Register contains data on all admissions to Danish psychiatric in-patient facilities, and from 1995, all contacts to outpatient psychiatric departments and visits to psychiatric emergency care units were included.

We included parents with a diagnosis of schizophrenia defined as schizophrenia, delusional disorder, or schizoaffective disorder coded by the International Classification of Diseases, 10th revision (ICD-10) or 8th revision (ICD-10: F20, F22, and F25 or ICD-8: 295, 297, 298.29, 298.39, 298.89, 298.99) or bipolar disorder (BP) (ICD-10: F30 and F31 or ICD-8: 296.19, 296.39) in the Danish registries. We defined the co-parent as the other biological parent without schizophrenia or bipolar disorder (the co-parents could per definition not have a diagnosis of schizophrenia or bipolar disorder recorded in the Danish registries). We labeled these parents SZ-co and BP-co. Parents from the control group and all co-parents could have any other mental disorder diagnosis. Both parents from the population-based control group were labeled PBC.

All participants provided written informed consent after having received both verbal and written information about the study. The study was approved by the Danish Data Protection Agency. The Danish Health Authority granted permission to retrieve the data from Danish registers. The study protocol was evaluated by the National Committee on Health Research Ethics and all procedures were performed according to their guidelines. However, according to Danish law, this type of study did not require ethical approval.

2.2. Procedures

We attempted to contact 943 out of 11 957 families who were eligible to participate in the study during the study period. Parents received a letter with a short description of VIA 7 by mail. If they did not respond to the letter, we contacted them by phone, text messages, or email. A huge effort was made to get in touch with each parent. Of the 943 families, 522 (55%) were enrolled in the VIA 7 study. Out of the 421 non-participating families, 172 did not respond, and 249 declined to participate. Representativity and possible selection bias of the VIA 7 cohort are described in detail elsewhere (Krantz et al., 2022).

The Affective Lability Scale - Short Form (ALS-SF) questionnaire was administered as part of a larger test battery which took around 3 days. The majority of assessments were conducted at the two research sites: the Psychosis Research Unit, Aarhus University Hospital, Risskov, Denmark, and at the Research Unit, Mental Health Centre Copenhagen, Copenhagen, Denmark. All assessors were psychologists, medical doctors, or nurses.

2.3. Measures

We used the questionnaire The Affective Lability Scale - Short Form (ALS-SF) to measure affective lability (Oliver and Simons, 2004). ALS-SF has been validated against the original Affective Lability Scale which consists of 54 items (Harvey et al., 1989). The ALS-SF consists of 18 items that are rated on a four-point Likert scale rating from 0 ("very uncharacteristic of me") to 3 ("very characteristic of me"). The scale consists of three subscales covering anxiety/depression, depression/elation, and anger and a total score. As advised in Oliver and Simons,

2004, the subscale scores were divided by the total number of items in the subscale. Higher scores in ALS-SF reflect elevated affective lability (Oliver and Simons, 2004).

2.4. Statistical analysis

The study groups were compared on demographic characteristics using one-way analysis of variance (ANOVA) or Pearson's chi-squared test of independence. ANOVA was applied to test between-group differences as well as within-group differences of ALS total score and the three subscales. Effect sizes were calculated using Cohen's d (small, 0.2; medium, 0.5; and large, 0.7). Due to the risk of overcorrecting, we did not co-vary for socioeconomic status (education and employment), which is intrinsically associated with familial high risk group status. Multiple comparisons were handled using Tukey's multiple comparison test. All analyses were performed with Stata 15 statistical software. We used a significance level of 5%.

3. Results

3.1. Demographic characteristics

Our study included data from 872 biological parents (148 parents with SZ, 157 SZ-co, 98 parents with BP, 89 BP-co, and 359 PBC). Parents with SZ were significantly younger compared with parents with BP and PBC. SZ-co were significantly younger compared with parents with BP-co and PBC. Both SZ and BP, and SZ-co and BP-co were less often employed or studying compared to PBC. Further, parents with SZ had lower levels of education compared with BP and PBC, and SZ-co had lower levels of education compared with BP-co and PBC (Table 1).

3.2. Between-group differences

Parents with SZ had significantly higher scores on the ALS anger subscale, ALS anxiety/depression subscale, ALS depression/elation subscale, and ALS total score compared to PBC with medium to large effect sizes. Parents with BP had significantly higher scores on the ALS anger subscale, ALS anxiety/depression subscale, ALS depression/elation subscale, and ALS total score compared to PBC with medium to large effect sizes. We found no significant difference between parents with SZ and parents with BP on the three subscales and the total score. Moreover, SZ-co had significantly higher scores on the ALS anxiety/depression subscale, ALS depression/elation subscale, and ALS total score compared to PBC with small effect sizes, but not on the ALS anger subscale. BP-co did not differ significantly from PBC on any of the three subscales or the total score and SZ-co did not differ significantly from BP-co on any of the subscales or the total score (Table 2 and Fig. 1).

3.3. Within-group differences

SZ-co had significant lower scores on ALS anger subscale, ALS anxiety/depression subscale, ALS depression/elation subscale, and ALS total score compared to parents with SZ. Moreover, BP-co had significant lower scores on ALS anger subscale, ALS anxiety/depression subscale, ALS depression/elation subscale, and ALS total score compared to parents with BP (Table 3 and Fig. 1).

4. Discussion

Confirming our first hypothesis, parents with SZ and parents with BP both had higher levels of affective lability compared to PBC. Furthermore, parents with SZ did not differ from parents with BP in their levels of affective lability. These results extend the very sparse research in the area of affective lability and SZ (Høegh et al., 2020; Høegh et al., 2021) and confirm that affective lability is an equally relevant clinical feature in BP and in SZ. In individuals with BP affective lability is seen as a central component of the disorder (Aminoff et al., 2012) but our results signify that increased affective lability is a shared feature by SZ and BP and thereby a transdiagnostic factor. The etiology of SZ and BP is not fully understood and there is evidence of genetic overlap between SZ

Table 1
Demographic characteristics of parents with schizophrenia, bipolar disorder, and their co-parents, and population-based controls.

	SZ	BP	PBC	*P-value* Pairwise comparisons		
				SZ vs. PBC	BP vs. PBC	BP vs. SZ
Parents, N	148	98	185	–	–	–
Female, N (%)	96 (64.9)	59 (60.2)	107 (57.8)	0.192	0.701	0.459
Age at inclusion, mean (SD)	38.00 (6.04)	40.20 (6.10)	40.60 (4.80)	**<0.000**	0.843	**<0.007**
Employed or studying, N (%) (*N* = 425)	75 (52.45)	56 (57.73)	170 (91.89)	**<0.000**	**<0.000**	0.420
Education, N (*N* = 481)	140	97	180			
Primary/ lower secondary, N (%)	38 (27.14)	7 (7.22)	7 (3.89)	**<0.000**	0.347	**<0.000**
Upper secondary, vocational, short cycle tertiary, N (%)	61 (43.57)	41 (42.27)	88 (48.89)			
Bachelor degree, equivalent or higher, N (%)	41 (29.29)	49 (50.52)	85 (47.22)			
Co-parents, N	**SZ-co** 157	**BP-co** 89	**PBC** 174	**SZ-co vs. PBC**	**BP-co vs. PBC**	**BP-co vs. SZ-co**
Female, N (%)	77 (49.04)	46 (51.69)	79 (45.10)	0.507	0.334	0.691
Age at inclusion, mean (SD)	38.74 (6.3 6)	41.17 (5.39)	40.81 (4.26)	**0.002**	0.860	**0.002**
Employed or studying, N (%) (*N* = 414)	116 (75.82)	76 (85.39)	165 (95.93)	**<0.000**	**0.002**	0.076
Education, N (*N* = 410)	151	87	172			
Primary/ lower secondary, N (%)	22 (14.57)	3 (3.45)	9 (5.23)	**0.004**	0.352	**<0.001**
Upper secondary, vocational, short-cycle tertiary, N (%)	78 (51.66)	35 (40.23)	82 (47.67)			
Bachelor degree, equivalent or higher, N (%)	51 (33.77)	49 (56.32)	81 (47.09)			

SZ = Parents with a diagnosis of schizophrenia, BP = Parents with a diagnosis of bipolar disorder, SZ-co = co-parents to parents with a diagnosis of schizophrenia, BP-co = co-parents to parents with a diagnosis of bipolar disorder, PBC = population-based control group.
Results from one-way analysis of variance or Pearson's chi-squared test of independence. P-values marked in bold are considered statistically significant.

Table 2
Between-group differences in Affective Lability Scale – Short form (ALS-SF) on parents with schizophrenia, bipolar disorder, and their co-parents, and population-based controls.

						PAIRWISE COMPARISONS					
	SZ	BP	PBC	SZ - co	BP - co	SZ vs. PBC	BP vs. PBC	SZ vs. BP	SZ - co vs. PBC	BP - co vs. PBC	SZ - co vs. BP - co
TEST/VARIABLE	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	***P***	***P***	***P***	***P***	***P***	***P***
	(SD)	**(SD)**	**(SD)**	**(SD)**	**(SD)**	***d***	***d***	***d***	***d***	***d***	***d***
ALS ANGER	0.72	0.74	0.39	0.51	0.38	**<0.001**	**<0.001**	0.999	0.249	0.999	0.455
	(0.72)	(0.79)	(0.50)	(0.62)	(0.43)	0.57	0.60	−0.03	0.22	−0.03	0.24
ANXIETY/DEPRESSION	0.94	1.05	0.30	0.54	0.35	**<0.001**	**<0.001**	0.678	**0.002**	0.965	0.207
	(0.83)	(0.92)	(0.47)	(0.77)	(0.48)	1.07	1.27	−0.13	0.42	0.11	0.28
DEPRESSION/ELATION	1.06	1.20	0.50	0.71	0.54	**<0.001**	**<0.001**	0.444	**0.003**	0.987	0.200
	(0.70)	(0.71)	(0.53)	(0.66)	(0.53)	0.95	1.20	−0.19	0.37	0.07	0.28
ALS TOTAL	0.93	1.02	0.41	0.61	0.44	**<0.001**	**<0.001**	0.623	**<0.001**	0.993	0.124
	(0.63)	(0.66)	(0.43)	(0.60)	(0.43)	1.04	1.25	−0.15	0.40	0.06	0.31

SZ = Parents with a diagnosis of schizophrenia, BP = Parents with a diagnosis of bipolar disorder, SZ-co = co-parents to parents with a diagnosis of schizophrenia, BP-co = co-parents to parents with a diagnosis of bipolar disorder, PBC = population-based control group.
Results from one-way analysis of variance. Effect sizes were calculated using Cohen's d. P-values marked with bold are considered statistically significant.

and BP (Martin et al., 2018). Affective lability may help the further investigation of underlying transdiagnostic factors and the etiology of SZ and BP.

In support of our second hypothesis, we found that co-parents to parents with SZ had higher levels of affective lability compared to PBC. In contrast to this, co-parents to parents with BP did not differ from controls. This was somewhat surprising as affective lability is a core feature of bipolar disorder and in relation to this, it could be speculated that it would be elevated in their partners too. This study is to our knowledge the first study examining levels of affective lability in co-parents to parents with SZ and BP and our findings can be understood in light of nonrandom mating, which has previously been examined in the current cohort (Greve et al., 2021; Jefsen et al., 2022). Nonrandom mating may result from the initial selection of a mate (assortment), and/or by couples becoming increasingly alike when living together (convergence) (Bulik-Sullivan et al., 2015; Vinkhuyzen et al., 2012). From our results, we are not able to examine whether the levels of affective lability are developed through the relationship between the parents, maybe affected by potential mental illness, and/or if the parents both had higher levels of affective lability before entering their relationship. More research with other study designs is needed to explore this association.

Nonetheless, elevated affective lability in parents is of special importance in the context of child-rearing. It is reasonable to assume that high levels of affective lability are related to difficulties with parental role functioning and that elevated levels of affective lability in parents thus may affect parenting, the emotional atmosphere in the home and thus child development (Lunkenheimer et al., 2007). If a parent is ill, the care for the child will often – at least in periods - depend on the co-parent. Thus, elevated affective lability in parents and co-parents may be a potential risk factor adding to the totality of risk factors possibly facing the children in these families in addition to the effects of the genetic risk.

4.1. Strengths and limitations

To our knowledge, The Danish High Risk and Resilience Study VIA 7 is the largest sample to date examining affective lability in both biological parents to 7-year-old children with one parent with either SZ or BP and PBC. Using this representative population-based cohort is a major strength of our study. Despite this strength, our findings should also be interpreted in the context of limitations. First, the current study was cross-sectional, and we are therefore unable to determine any causal relations for example whether the identified non-random mating was due to assortment or convergence. Second, due to the study design, where we only investigated parents (i.e. selection into parenthood), our results cannot be generalized to all individuals with schizophrenia or bipolar disorder as individuals with severe mental illness have fewer children compared with the general population (Laursen and Munk-Olsen, 2010; Power et al., 2013). Also, compared to childless individuals with schizophrenia, parents with schizophrenia are more likely to have had better premorbid social adjustment and to become ill at a later age, which is known to be associated with less severe outcome than for example early onset schizophrenia (Mowbray et al., 2005; Tandon et al., 2008; Pedersen et al., 2014). Furthermore, we have not measured levels of mood symptoms for all included parents, and therefore we cannot rule out, that mood symptoms such as depressive symptoms could increase the level of affective lability. It is reasonable to assume that the presence of a mental disorder in the index parent (for example schizophrenia) could affect his or her partner (SZ-co parent) and spur the development of symptoms more sensitive to stress (for example depressive symptoms). This is supported by results from an earlier study using the same cohort where we found that individuals who have children by partners with schizophrenia more often present with a depression diagnosis (Greve et al., 2021). Lastly, as ALS-SF is a self-report measure, the risk of recall- and response bias cannot be ruled out.

5. Conclusion

In this unique and large population-based sample, we showed that parents with SZ and parents with BP had higher levels of affective lability compared with PBC. Parents with SZ and BP did not differ in their levels of affective lability. These findings add important knowledge to the understanding of affective lability as a shared feature in SZ and BP. Furthermore, co-parents to parents with SZ had significantly higher levels of affective lability compared to PBC. We did not find this difference in BP-co compared to PBC. These findings should be considered in future investigation of potential risk factors for children in families with parental SZ and BP.

Funding

This work was supported by the Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH) (grant number R248-2017-2003, R155-2014-1724, R102-A9118), Aarhus University, Aarhus University Hospital Psychiatry, the Mental Health Services of the Capital Region of Denmark and the Beatrice Surovell Haskell Fund for Child Mental Health Research of Copenhagen.

The sources of funding had no involvement in the study design, data collection, data analysis, interpretation, writing of the manuscript, or decision to submit the manuscript for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit it for publication. All authors have

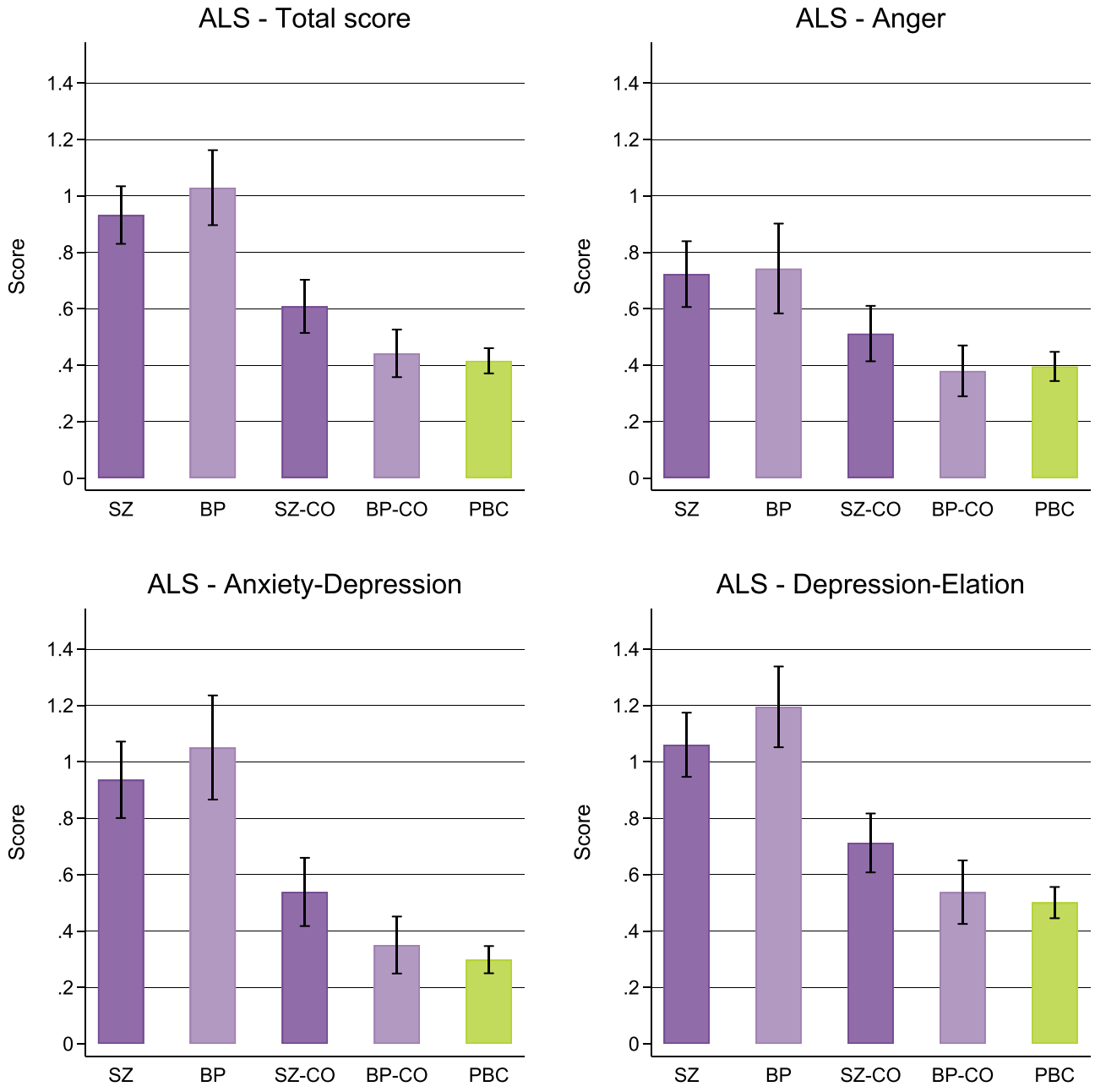

Fig. 1. Total mean score and subscale scores on Affective Lability Scale – Short form (ALS-SF) on parents with schizophrenia, bipolar disorder, and their co-parents, and population-based controls.
The total mean score and the subscale scores were divided by the total number of items in the scale and presented with 95% confidence intervals. SZ = Parents with a diagnosis of schizophrenia, BP = Parents with a diagnosis of bipolar disorder, SZ-co = co-parents to parents with a diagnosis of schizophrenia, BP-co = co-parents to parents with a diagnosis of bipolar disorder, PBC = population-based control group.

Table 3
Within-group differences in Affective Lability Scale – Short form (ALS-SF) between parents with schizophrenia or bipolar disorder, and their co-parents.

TEST/VARIABLE	SZ-co vs SZ			BP-co vs. BP		
	Δ	**95% CI**	***P***	**Δ**	**95% CI**	***P***
ALS ANGER	−0.21	(−0.40; −0.02)	**0.018**	−0.36	(−0.60; −0.12)	**<0.001**
ANXIETY/DEPRESSION	−0.40	(−0.61;−0.19)	**<0.001**	−0.70	(−0.97; −0.43)	**<0.001**
DEPRESSION/ELATION	−0.35	(−0.54; −0.16)	**<0.001**	−0.66	(−0.90; −0.41)	**<0.001**
ALS TOTAL	−0.32	(−0.49; −0.16)	**<0.001**	−0.59	(−0.80; −0.38)	**<0.001**

SZ = Parents with a diagnosis of schizophrenia, BP = Parents with a diagnosis of bipolar disorder, SZ-co = co-parents to parents with a diagnosis of schizophrenia, BP-co = co-parents to parents with a diagnosis of bipolar disorder.
Results from one-way analysis of variance. P-values marked with bold are considered statistically significant.

approved the final version of the manuscript.

CRediT authorship contribution statement

Nanna Lawaetz Steffensen: Conceptualization, Formal analysis, Methodology, Writing – original draft. **Nicoline Hemager:** Investigation, Supervision, Writing – review & editing. **Anette Faurskov Bundgaard:** . **Ditte Lou Gantriis:** Investigation, Writing – review & editing. **Birgitte Klee Burton:** Investigation, Writing – review & editing. **Ditte Ellersgaard:** Investigation, Writing – review & editing. **Anders Helles Carlsen:** Formal analysis, Methodology, Supervision. **Vibeke Bliksted:** Supervision, Project administration, Writing – review & editing. **Kerstin J. Plessen:** Conceptualization, Project administration, Writing – review & editing. **Jens Richardt Møllegaard Jepsen:** Conceptualization, Investigation, Project administration, Writing – review & editing. **Merete Nordentoft:** Supervision, Conceptualization, Funding acquisition, Project administration, Writing – review & editing. **Anne A.E. Thorup:** Supervision, Conceptualization, Investigation, Project administration, Writing – review & editing. **Ole Mors:** Supervision, Conceptualization, Funding acquisition, Project administration, Writing – review & editing. **Aja Neergaard Greve:** Conceptualization, Supervision, Formal analysis, Investigation, Methodology, Project administration, Writing – original draft.

Declaration of Competing Interest

None.

Acknowledgments

The authors would like to express their gratitude to the dedicated families participating in the study; to M. Skjærbæk, K. Spang, C. Christiani, A. Søndergaard, M. Gregersen, A. Ranning, H. Jensen, M. Melau and C. Gregersen for contributing to data collection; to C. Bøcker Pedersen and M. Giørtz Pedersen for retrieving the register extract; to M. Chaine for help with data management; and to P.B. Mortensen, T. Werge, D. Hougaard and A. Børglum for collaboration in iPSYCH.

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