Adolescent social functioning deficits in association with adoptive family functioning and genetic risk for schizophrenia spectrum disorders: the Finnish Adoptive Family Study of Schizophrenia

Abstract

Social functioning deficits (SFDs) during adolescence represent potential vulnerability indicators to schizophrenia spectrum disorders, but little is known about both how family environmental and genetic factors contribute to SFDs. The aim of this study was to examine the association of adoptees' adolescent social functioning with adoptive family functioning and adoptees' high (HR) or low (LR) genetic risk for schizophrenia spectrum disorders. The present subsample from the nationwide Finnish Adoptive Family Study of Schizophrenia included 88 HR and 83 LR adoptees. Adolescent social functioning was assessed using UCLA Social Attainment Survey (UCLA SAS). Assessment of adoptive family functioning was based on Global Family Ratings (GFRs). Results indicated that dysfunctional family processes and high genetic risk for schizophrenia spectrum disorders contributed approximately equally to adoptees' adolescent social functioning. Our findings underscore the importance of functional family processes in adolescent social functioning, particularly in individuals at high genetic risk for severe psychiatric disorder.

Keywords: Social functioning; adolescence; family functioning; genetic risk; adoption study

Introduction

In schizophrenia, social functioning deficits (SFDs) such as difficulties in establishing, initiating, and maintaining interpersonal relationships, are among the key factors that make the disorder disabling (e.g., Martin et al., 2015). It is well established that SFDs are often observable years before onset of illness, particularly during adolescence (e.g., Velthorst et al., 2017). SFDs are not solely explained by subclinical signs and symptoms of prodromal phase, symptoms of the

manifested disorder or the effects of medication or hospitalizations, but may also represent vulnerability indicators (Hooley, 2010). Moreover, studies have consistently observed more adolescent SFDs in offspring at high genetic risk for schizophrenia spectrum disorders (high-risk offspring) than in low-risk controls (e.g., Glatt et al., 2006; Hans et al., 2000; Horton et al., 2014; Tikkanen et al., 2020).

Although findings suggest a strong link between SFDs and high genetic risk, the role of the second integral component, rearing environment, has remained unresolved. Only a few SFD studies (Hatzimanolis et al., 2020; Kilian et al., 2017; Matheson et al., 2017) have considered both family environmental (parental socioeconomic status, maltreatment, trauma) and genetic factors. Moreover, the findings from these studies have been mixed, leaving it unclear how genetic risk, family environment and their possible interaction may influence SFDs. In SFD studies, no attention has been paid to family functioning (e.g., interaction, relationships, emotional atmosphere within the family), although its importance has been emphasized in the development of schizophrenia spectrum disorders and other psychiatric disorders, particularly in high-risk offspring (Myllyaho et al., 2019; Tienari et al., 2004; Wahlberg et al., 2004). Therefore, family functioning should be considered in the research of SFDs as vulnerability indicators to such disorders.

Importantly, when a child has a first-degree relative with a schizophrenia spectrum disorder, the likelihood of stressful and dysfunctional family environment increases (Walder et al., 2014). Thus, when the offspring are reared by their biological parents, making conclusions on how family functioning and genetic risk for schizophrenia spectrum disorders contribute to SFDs is difficult, if not impossible. Adoption studies where the offspring are reared by adoptive instead of biological parents may provide an optimal method for studying these deficits. The existing adoption studies have highlighted the role of genetic factors (Kendler et al., 1982) and gene-environment interaction (Siira et al., 2007) in social difficulties. However, these SFD studies have not included measures from the family environment or focused specifically on social functioning, respectively.

The vulnerability-stress model (Nuechterlein and Dawson, 1984; Rosenthal, 1970; Zubin and Spring, 1977) has been widely used in understanding the development of psychiatric disorders, but also the expression of vulnerability factors. It can be viewed as an epigenetic process where the genetic component of vulnerability is shaped in transactions with the physiological and psychosocial environment throughout an individual's development (Smigielski et al., 2020; Wynne, 1978, 1984). The vulnerability is thought to be present at birth but may not manifest until later. Moreover, the model recognizes adolescence as a critical period for the expression of this vulnerability and posits deficits in social functioning as one of its central indicators (Cheng et al., 2016; Nuechterlein and Dawson, 1984).

To our knowledge, no study to date has examined the adolescent social functioning of adopted-away offspring in genetic high and low risk for schizophrenia spectrum disorders and included measures of the family environment where the offspring have been raised. The present study from the Finnish Adoptive Family Study of Schizophrenia (Tienari et al., 2000) utilizes a high-risk approach and an adoptive study design, providing a unique possibility to control the rearing environment, and separately, to study the impact of family environmental and genetic factors on adoptees' social functioning. Also, during extensive visits to each adoptive family home, the adoptive families were assessed with structured methods including objective observations, making it possible to study the rearing environment in greater detail compared to earlier SFD studies. The aim of the present study was to examine the association of adoptees' adolescent social functioning with adoptive family functioning and adoptees' genetic risk for schizophrenia spectrum disorders. We hypothesized that deficits in adoptees' adolescent social functioning are associated with dysfunctional processes of the adoptive family, and high genetic risk for schizophrenia spectrum disorders. We further hypothesized that these deficits would be emphasized in genetic high-risk adoptees reared in adoptive families with dysfunctional family processes compared to

high-risk adoptees reared in adoptive families with functional family processes and compared to their corresponding low-risk adoptees.

Methods

Participants

This study is based on nationwide data from the Finnish Adoptive Family Study of Schizophrenia. Briefly, the study population was based on the hospital records of all women admitted to Finnish psychiatric hospitals during the years 1960–1979 (n = 19,447) and who had been diagnosed with schizophrenia or paranoid psychosis at least once. The women who had given one or more offspring (high-risk adoptees) for adoption were identified. Adoptees adopted after the age of four, adopted by a relative, or adopted abroad were excluded. The adoptive parents were eligible for the study with no diagnostic exclusion criteria. The genetic high-risk (HR) adoptees and their adoptive families were matched demographically with low-risk control (LR) adoptees and their adoptive families based on the age and sex of the adoptee and adoptive parents, age of the adoptee at placement to the adoptive family, and socioeconomic status and family structure of the adoptive family (Tienari et al., 1981). The LR adoptees' biological mothers either had no psychiatric diagnoses or had diagnoses of psychiatric disorders outside the schizophrenia spectrum.

The final study population included 190 HR adoptees whose biological mothers had verified DSM-III-R (American Psychiatric Association, 1987) diagnoses of schizophrenia spectrum disorders: schizophrenia, schizotypal, schizoid, paranoid and avoidant personality disorder, schizoaffective, schizophreniform, delusional disorder and psychotic disorder not otherwise specified, and bipolar and depressive disorders with psychotic features (Kendler et al., 1996). The control sample comprised 192 LR adoptees. The initial psychiatric assessment of the adoptees was

made according to the DSM-III-R criteria and included personal interviews, a review of hospital records and registers, and interviews with family members and other informants. The kappa coefficient for interrater diagnostic reliability was 0.80. The design, sampling, and diagnostic procedures have been described in detail earlier (see Tienari et al., 1987, 2000, 2003, 2004). The study design of Finnish Adoptive Family Study of Schizophrenia was approved by Oulu University Hospital Ethics Committee.

This study comprised those adoptees for whom information on the UCLA Social Attainment Survey was available for at least four out of seven items of the survey. Thus, the present subsample consists of 171 (88 HR and 83 LR) adoptees with a minimum age of 16 years. The data for UCLA Social Attainment Survey was available for 88/190=46.3% HR adoptees and 83/192=43.2% LR adoptees. The initial psychiatric diagnoses of the adoptees distributed as follows: schizophrenia spectrum disorders (schizophrenia, schizoaffective disorder, schizophreniform psychosis, delusional disorder, avoidant and schizotypal personality disorder, and bipolar disorder with psychosis), HR n=7, LR n=1; personality disorders other than schizophrenia spectrum disorders (antisocial, borderline, narcissistic, histrionic and dependent personality disorders, and personality disorder not otherwise specified), HR n=8, LR n=6; mood disorders other than schizophrenia spectrum disorders (dysthymic disorder and depression not otherwise specified), HR n=4, LR n=7; anxiety disorders, HR n=5, LR n=3; substance use disorders, HR n=2, LR n=0; other psychiatric disorders (eating disorders and somatoform disorders), HR n=2, LR n=1.

Procedure

In the initial phase of the study, starting in 1977, the adoptive families were assessed during home visits. The interviewers were experienced psychiatrists blinded to the adoptees' genetic risk status. The intensive and comprehensive interview procedure of a family usually lasted two days. The duration of the visits and the familiar environment for the family allowed for a wide range of observations, including nonverbal evidence of tension between family members and other habitual

patterns of interaction (Wynne et al., 2006). First, the family was interviewed as a whole, followed by an interview with the parental couple. Finally, the parents and adoptees were interviewed individually. The study participants also underwent family, couple and individual observations and several psychological tests.

Measures

Global Family Ratings

Global Family Ratings (GFRs) (Tienari et al., 1987; Wynne et al., 2006) were used as a measure of adoptive family functioning. GFRs are based on semi-structured interviews and comprehensive and objective observations during the interview sessions. GRFs evaluate 1. Anxiety and its levels, 2. Boundaries between the individual family members, generations, and between the family and the outside world, 3. Parental coalition, 4. Quality of interaction, 5. Flexibility of homeostasis, 6. Transactional defenses, 7. Conflicts, 8. Empathy, 9. Power relations, 10. Reality testing, and 11. Basic trust within the family. Based on these domains, families were classified into five categories: 1) Healthy, 2) Mildly dysfunctional, 3) Neurotic, moderately dysfunctional, 4) Rigid, syntonic, and 5) Severely dysfunctional, chaotic families. All the interviews and test procedures were tape-recorded. The reliability assessment of ratings (kappa coefficient) between the interviewers was 0.72 (on a scale from 0 = poor to 1 = high concordance of ratings) and was ensured by several steps described earlier (Myllyaho et al., 2019; Tienari et al., 1987; Wynne et al., 2006)

Consistent with Myllyaho et al. (2019), the five GFRs categories were combined and re-labeled based on significant similarities between certain categories. Categories 1–2 were combined to describe “Families with functional processes” as both can be considered within the range of healthy and functional family processes. “Families with mildly dysfunctional processes” was

formed to include GFR category 3. Categories 4–5 were combined as “Families with dysfunctional processes”.

UCLA Social Attainment Survey

As part of the individual semi-structured interviews, adoptees’ social functioning during adolescence (ages 16–20) was assessed using the UCLA Social Attainment Survey (hereafter UCLA SAS) (Goldstein, 1978). UCLA SAS comprises seven items evaluating social functioning in peer and romantic relationships and involvement in activities. The items include: 1. Same-sex peer relationships, 2. Leadership in same-sex peer relationships, 3. Opposite-sex relations, 4. Dating history, 5. Sexual experience, 6. Outside activities and 7. Participation in organizations. Each item is scored on a 1–5 scale, with lower scores indicating poorer social functioning. The total scores, used to reflect Overall Social Functioning, range from 7 to 35. Consistent with earlier studies (Horan et al., 2006; Subotnik et al., 2000; Tikkanen et al., 2020), the seven items were combined into three categories: Peer Relationships (items 1–2), Romantic Relationships (items 3–5), and Involvement in Activities (items 6–7).

Statistical Methods

Statistical significance of group differences in categorical variables was assessed with Pearson’s Chi-square test or Fisher’s Exact test and in continuous variables with Student’s t-test and one-way analysis of variance. Analysis of covariance (ANCOVA) was used to examine the association of UCLA SAS scores with genetic risk and GFRs (as main effects) after controlling for adoptee’s gender and initial psychiatric status, social class of the adoptive family, adoptee’s age at placement in adoptive family (in months), and adoptee’s age at UCLA SAS assessment (in years). All tests were two-tailed and the limit for statistical significance was set at $p < .05$. IBM SPSS Statistics 26 software was used in analyses.

Results

A comparison of the baseline characteristics was made between the adoptees in the present subsample and the rest of adoptees in the original sample with minimum age of 16 years during the initial assessment, but of whom the information on the UCLA SAS was lacking. There were no statistically significant differences between these two samples in terms of the age of the adoptee at placement to the adoptive family, gender, genetic risk status or the initial psychiatric status of the adoptee, or the socioeconomic status of the adoptive family. A statistically significant difference between the present subsample and the excluded adoptees was found in the age [in years (SD)] of the adoptee during the initial assessment [24.91 (8.92) vs. 32.93 (8.78), $p < 0.001$]. The adoptees in the present subsample were younger compared to the excluded adoptees. A statistically significant difference was also found in the GFR categories [Families with functional processes: 47.1 % vs. 33.1 %, Families with mildly dysfunctional processes: 34 % vs. 24.6 %, Families with dysfunctional processes: 19 % vs. 42.4 %, $p < 0.001$]. The proportion of adoptees belonging to adoptive families with dysfunctional processes was lower in the present subsample.

Demographic characteristics are presented in **Table 1**. There were no statistically significant differences in the demographic characteristics between male and female adoptees.

/Insert Table 1 about here/

Table 2 shows that statistically significantly lower scores in Overall Social Functioning, Peer Relationships and Involvement in Activities were observed in adoptees reared in families with dysfunctional processes. HR adoptees scored significantly lower in Overall Social Functioning, Peer Relationships and Involvement in Activities compared to LR adoptees.

In male adoptees, statistically significant difference in Overall Social Functioning was observed between HR and LR adoptees. HR male adoptees scored lower compared to LR male

adoptees. No differences were found between the three family functioning categories in male adoptees. Statistically significantly lower scores in Overall Social Functioning, Peer Relationships and Involvement in Activities were observed in female adoptees reared in families with dysfunctional processes.

/Insert Table 2 about here/

As seen in **Table 3**, after adjusting for the covariates (adoptee's gender and initial psychiatric status, social class of the adoptive family, adoptee's age at placement to the adoptive family, and adoptee's age at UCLA SAS assessment), the variation of Overall Social Functioning and Peer Relationships scores was statistically significantly associated with family functioning (as main effect). Adoptees reared in families with dysfunctional and mildly dysfunctional processes received poorer UCLA SAS scores compared to adoptees reared in families with functional processes. The variation of UCLA SAS Overall Social Functioning, Peer Relationships, Romantic Relationships, and Involvement in Activities scores was statistically significantly associated with genetic risk (as main effect). HR adoptees scored lower than LR adoptees. The analyses were repeated by excluding the adoptees with initial psychiatric diagnoses and the major results did not change (results available on request). In an additional ANCOVA analysis, the interaction between family functioning and genetic risk was tested but no significant interaction effect was found.

/Insert Table 3 about here/

As visualized in **Figure 1**, adoptees reared in families with dysfunctional and mildly dysfunctional processes had lower Overall Social Functioning scores than adoptees reared in families with functional processes. HR adoptees had lower Overall Social Functioning scores in all three family functioning categories compared to LR adoptees, with statistically significant difference found in families with functional processes ($p = 0.035$). Additional analysis showed that after combining the two categories of more dysfunctional family processes (families with

dysfunctional and mildly dysfunctional processes) the difference between LR and HR adoptees was statistically significant (p = 0.023). In addition, there was a statistically significant difference (p = 0.043) between LR adoptees in families with functional processes and LR adoptees in the two dysfunctional family processes categories. The difference between their corresponding HR adoptees was marginally significant (p = 0.082)

/Insert Figure 1 about here/

Discussion

Social functioning deficits (SFDs) during adolescence represent potential indicators of vulnerability to schizophrenia spectrum disorders, but little is known about how both family environmental and genetic factors contribute to SFDs. In this study we were able to examine adolescent social functioning in association with adoptive family functioning and adoptees' genetic risk for schizophrenia spectrum disorders. This research information can be utilized in identifying at-risk groups and targets for prevention and in developing preventive strategies.

In our study, in both HR and LR adoptees, poorer Overall Social Functioning and Peer Relationships during adolescence were associated with dysfunctional processes of the adoptive family. This is concordant with previous findings that offspring generally show decreased friendship quality and participation in social interactions and increased loneliness when the family environment is characterized by dysfunctional interpersonal patterns, lack of expressed warmth and empathy, and conflicts (e.g., Mak et al., 2018; Repetti et al., 2002). In our study, these features were also included in the definition of adoptive families with dysfunctional family processes. Thus, in the present study, the role of family processes was highlighted in the development of social functioning deficits in adolescence.

Regarding genetic risk, poorer scores in Overall Social Functioning and in all social functioning domains (Peer Relationships, Romantic Relationships, Involvement in Activities) were associated with high genetic risk for schizophrenia spectrum disorders. This is consistent with findings from previous high-risk studies suggesting that high-risk adolescents display SFDs focused on relationships with other young people and participation in social activities (Dworkin et al., 1994; Hans et al., 2000). Compared to these high-risk studies, however, in the present study the adoption study design allowed us to control the rearing environment of the adoptive families. Thus, our findings add weight to previous suggestions that adolescent SFDs are associated with high genetic risk for schizophrenia spectrum disorders (e.g., Glatt et al., 2006) and suggest that SFDs during adolescence may represent vulnerability indicators in high-risk populations.

The question remains how adoptive family functioning may influence the expression of SFDs in HR adoptees in particular. As described above, both HR and LR adoptees displayed poorer Overall Social Functioning when the family processes were dysfunctional. However, HR adoptees were found to display poorer Overall Social Functioning compared to LR adoptees in all family functioning categories (families with functional, mildly dysfunctional, and dysfunctional processes). To our knowledge, this finding has not been documented in the published SFD research. This finding extends our understanding of SFDs by suggesting that not only do high-risk adoptees display poorer social functioning compared to low-risk adoptees, but the same pattern can also be seen in all levels of family functioning. In other words, our findings suggest that SFDs are not expressed in high-risk adoptees only in the context of a dysfunctional, or predisposing, rearing environment. From a positive standpoint, although especially low-risk adoptees seem to benefit from functional family processes in terms of their social functioning, functional family processes also seem to promote the social functioning of high-risk adoptees. Therefore, healthy family functioning might possibly have a protective effect against the development of psychiatric disorders in genetic high-risk adoptees. This, however, remains speculative in the present study.

While there may be many explanations for the development in SFDs in HR adoptees, one plausible link may be found in social cognition (emotional and cognitive factors underlying social behavior; Fulford et al., 2018). First, it has been suggested that in high-risk individuals, genetically influenced disruptions to certain neural mechanisms may result in difficulty in interpreting and attributing intentions and emotions of others (Dodell-Feder et al., 2014). In social interactions, this might lead to increased interpersonal conflict and stress, compromised social network, and withdrawal, for instance. Accumulating evidence suggests that social cognition deficits are potential endophenotypes for schizophrenia (Tikka et al., 2020). Endophenotypes are defined as trait-like deficits that are found in patients with the disorder, are present independent of its state, are also found in unaffected family members at higher rates than in general population, and are heritable (Gottesman and Gould, 2003). Second, family functioning also influences social cognition, such as emotion regulation abilities, which are essential for positive social interactions. For instance, family conflicts may have a negative influence on adolescents' ability to cope with negative emotions in social situations, leading to decreased quality in their social relationships (Schwarz et al., 2012). Thus, given that in our study SFDs were emphasized in genetic high-risk adoptees reared in adoptive families with dysfunctional processes, family environmental and genetic influences on social cognition may represent one possible pathway explaining these findings.

Interestingly, gender-specific bivariate analyses revealed that Overall Social Functioning significantly distinguished HR males from LR males, whereas in female adoptees a difference in Overall Social Functioning was prominently related to the level of family functioning of the adoptive family. Although conclusions should be made cautiously, earlier findings suggest heightened sensitivity towards family stressors especially in adolescent females (Chung et al., 2009). More specifically, compared to males, adolescent females may experience difficulties within the family (family conflicts, low parental warmth) as more stressful, and may be more likely to display internalizing behavior (e.g., social withdrawal) (Schleider and Weisz, 2017). However,

further research is needed for deeper understanding of possible gender differences regarding family functioning and genetic risk for schizophrenia spectrum disorders.

Strengths and limitations

The present subsample was derived from the nationwide and globally unique data of the Finnish Adoptive Family Study of Schizophrenia. The major strength of the present study lies in the adoptive study design, which allowed us to examine both genetic and family environmental factors. Furthermore, the adoptive families were evaluated comprehensively by experienced psychiatrists during extensive visits to the adoptive families. This allowed for a wide range of procedures, including a detailed assessment of adoptive family functioning (e.g., boundaries between family members, quality of interaction, expressed empathy, conflicts) with objective observations. Furthermore, adoptees' adolescent social functioning was assessed using the UCLA SAS, a measure used consistently in the assessment of social functioning in schizophrenia (Horan et al., 2006; Subotnik et al., 2000). In addition, representative of a wider population, the biological control mothers either had no psychiatric diagnoses or had diagnoses of psychiatric disorders outside the schizophrenia spectrum.

Regarding limitations, the current study sample covered 56% of the original sample aged 16 or above. The present subsample differed statistically significantly from the excluded sample only in terms of age and adoptive family functioning at initial assessment showing that adoptees were younger and the proportion of those belonging to adoptive family with dysfunctional processes was lower compared to the sample of excluded adoptees. The impact of these variables to the UCLA SAS scores as well as other variables (the age at placement to the adoptive family, gender, genetic risk and the initial psychiatric status of the adoptees, the socioeconomic status of the adoptive family) were statistically controlled in the covariance analyses. Furthermore, the GFRs, which were used as a measure of adoptive family functioning, do not assess possible changes in family functioning that may have occurred during adoptees' upbringing (Myllyaho et al., 2019). However,

many studies in the Finnish Adoptive Family Study of Schizophrenia have shown stability in family functioning related factors, including communication (e.g., Roisko et al., 2011). Some adoptees in our study had already passed the age assessed in UCLA SAS (16–20 years), raising the possibility of recall bias. The adoptees were, however, relatively young during the assessment (mean age approximately 25 years). This, on the other hand, might have raised the risk of recency bias in which participants give more emphasis to the most recent events. Also, UCLA SAS measures romantic relationships only with the opposite sex, and therefore does not acknowledge possible same-sex relationships. Furthermore, it is possible that including biological mothers with psychiatric diagnoses outside the schizophrenia spectrum in the control group might have attenuated the effect of genetic risk. Also, the information regarding biological fathers was limited and was found to be unreliable in many cases for which they were not included in the study. Regarding the design of the present study, it is noteworthy that the adoption-study design does not make it possible to control for prenatal environment. Finally, the sample was relatively small, raising the possibility of chance findings (Type I error) and some findings not being detected (Type II error).

Conclusion

This study has added new insights to the knowledge of social functioning deficits (SFDs) as possible vulnerability indicators for psychiatric disorders as we were able to study the association of adolescent social functioning with both family functioning and genetic risk for schizophrenia spectrum disorders. In our study, dysfunctional family processes and high genetic risk for schizophrenia spectrum disorders contributed approximately equally to adoptees' adolescent social functioning. Our findings underscore that identifying risk factors related to family processes may be important for early prevention purposes, especially in individuals at high genetic risk for severe psychiatric disorder. Attention should also be directed to the importance of other social environments (e.g., school) in promoting the social development and functioning of children and adolescents while taking into account the benefits of individual psychosocial interventions. Future

studies should aim to examine the role of different environmental factors in SFDs, the possible mechanisms underlying them, and the longitudinal associations between SFDs and psychiatric morbidity.

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Figure legends:

FIGURE 1. Genetic high (HR) and low-risk (LR) adoptees' UCLA Social Attainment Survey (SAS) Overall Social Functioning and standard errors according to their adoptive family functioning based on ANCOVAs and adjusted for the covariates (gender and initial psychiatric status of the adoptee, social class of the adoptive family, adoptee's age at placement to the adoptive family, and adoptee's age at UCLA SAS assessment).

Note: * $p < 0.05$. Lower UCLA SAS scores indicate poorer social functioning.