Psychiatry Research 207 (2013) 203–211

Contents lists available at SciVerse ScienceDirect

Psychiatry Research

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

Parental psychiatric disorders and autism spectrum disorders

Elina Jokiranta [a,*], Alan S. Brown [b], Markus Heinimaa [c], Keely Cheslack-Postava [d], Auli Suominen [a], Andre Sourander [a,b,e]

[a] Department of Child Psychiatry, University of Turku and Turku University Hospital, Turku, Finland
[b] Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York State Psychiatric Institute, Mailman School of Public Health of Columbia University, New York, NY, USA
[c] Department of Psychiatry, University of Turku, Turku, Finland
[d] Department of Epidemiology, Mailman School of Public Health of Columbia University, New York, NY, USA
[e] RKBU, Faculty of Health Sciences, University of Tromso, Norway

ARTICLE INFO

Article history:
Received 16 January 2012
Received in revised form
15 November 2012
Accepted 10 January 2013

Keywords:
Schizophrenia
Affective
Childhood autism
Asperger's syndrome
Pervasive developmental disorders—unspecified
Risk factors
Epidemiology

ABSTRACT

The present population-based, case-control study examines associations between specific parental psychiatric disorders and autism spectrum disorders (ASD) including childhood autism, Asperger's syndrome and pervasive developmental disorder (PDD-NOS). The cohort includes 4713 children born between 1987 and 2005 with diagnoses of childhood autism, Asperger's syndrome or PDD-NOS. Cases were ascertained from the Finnish Hospital Discharge Register, and each was matched to four controls by gender, date of birth, place of birth, and residence in Finland. Controls were selected from the Finnish Medical Birth Register. Parents were identified through the Finnish Medical Birth Register and Finnish Central Population Register. Parental psychiatric diagnoses from inpatient care were collected from the Finnish Hospital Discharge Register. Conditional logistic regression models were used to assess whether parents' psychiatric disorders predicted ASD after controlling for parents' age, smoking during pregnancy and weight for gestational age. In summary, parental schizophrenia spectrum disorders and affective disorders were associated with the risk of ASD regardless of the subgroup. PDD-NOS was associated with all parental psychiatric disorders investigated. Further studies are needed to replicate these findings. These results may facilitate the investigation of shared genetic and familial factors between ASD and other psychiatric disorders.

1. Introduction

Autism spectrum disorders (ASD) have been considered highly heritable (Folstein and Rutter, 1977; Steffenburg et al., 1989; Bailey et al., 1995; Lichtenstein et al., 2010), even though environmental factors may account for at least some of the variance to develop ASD (Hallmayer et al., 2011). In a recent study, Hallmayer et al. (2011) demonstrated that approximately 55% of the variance in liability to ASD may be accounted for by environmental factors, though many studies show a much stronger genetic contribution. The most common subgroups of ASD are childhood autism, Asperger's syndrome and pervasive developmental disorders—unspecified (PDD-NOS) (World Health Organization, 1992). The diagnostic criteria for childhood autism include abnormalities in language, reciprocal social interactions, and the presence of a restricted repertoire of behavior and interests. The symptoms are required to emerge before age three to fulfill the diagnostic criteria (World Health Organization, 1992). Intellectual disability and cognitive problems are common in childhood autism. The diagnostic criteria for Asperger's syndrome include deficits in social interaction and behavior, while language development and intellectual capacity are required to be normal. Asperger's syndrome is seldom diagnosed before age seven. The diagnostic criteria for PDD-NOS are heterogeneous and less well defined. These children have multiple developmental delays in cognitive functioning, social interactions, motor skills and learning, but the symptomatology does not fulfill the criteria for any other ASD subgroup.

Clinical studies have demonstrated that psychiatric disorders are more common among relatives of children with ASD (Bolton et al., 1998; Piven and Palmer, 1999; Bölte et al., 2007; Mouridsen et al., 2007; Ingersoll et al., 2011). This has led to the assumption that ASD and several other psychiatric disorders may share common genetic/familial factors (Daniels et al., 2008). However, only three population-based studies have examined the association between

Abbreviations: ASD, Autism spectrum disorder; PDD-NOS, Pervasive developmental disorder, unspecified; FMBR, Finnish Medical Birth Register; FHDR, Finnish Hospital Discharge Register; CPR, Finnish Central Population Register; FIPS-A, Finnish Prenatal Study of Autism and Autism Spectrum Disorders; ICD, International Classification of Diseases; WGA, Weight for gestational age

* Correspondence to: Department of Child Psychiatry, University of Turku, Itäinen pitkäkatu 1 / Varia, 20014 Turku, Finland. Tel.: +358 2 333 7668; fax: +358 2 313 2412.
E-mail address: ekjoki@utu.fi (E. Jokiranta).

0165-1781/$ - see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.psychres.2013.01.005

ASD and parental psychiatric disorders (Larsson et al., 2005; Lauritsen et al., 2005; Daniels et al., 2008). Two of these studies assessed the relationship between ASD and specific parental psychiatric disorders (Larsson et al., 2005; Daniels et al., 2008) while in the third study parental psychiatric disorders were not specified (Lauritsen et al., 2005). In the Danish study (Larsson et al., 2005), parental schizophrenia, affective disorders and substance abuse were associated with childhood autism. That study, however, did not examine the association between childhood autism and maternal and paternal psychiatric disorders separately. In the Swedish study (Daniels et al., 2008) maternal and paternal schizophrenia spectrum, maternal depression, and non-psychotic personality disorders were associated with ASD. None of these previous studies (Larsson et al., 2005; Lauritsen et al., 2005; Daniels et al., 2008) have examined the associations among ASD subgroups (childhood autism, Asperger's syndrome and PDD-NOS).

The aims of the current study are: (1) to examine whether diagnosed psychiatric disorders are more common among mothers and fathers of children diagnosed with ASD compared to controls; and, (2) if so, to determine which psychiatric disorders are the most associated with ASD. Based on the previous studies showing a strong association between parental psychopathology and ASD we hypothesized that ASD would be associated with one or more parental psychiatric disorders, particularly with affective and schizophrenia spectrum disorders. We acknowledge the possible plan to subsume all autism spectrum disorders under one category in the DSM-V and therefore the analyses include a total ASD group combining childhood autism, Asperger's syndrome and PDD-NOS under one category. However, as at present there remain separate diagnostic criteria for each of these disorders, the examination is also made separately for these subgroups of ASD (childhood autism, Asperger's syndrome and PDD-NOS). Regardless of current diagnostic categories, ASD as a group encompass significant phenotypic heterogeneity, which is believed to stem from substantial etiologic heterogeneity. Observing associations with parental psychopathology that are consistent across subgroups would suggest factors common to both parental psychopathology and ASD as a whole, whereas differences in parental psychopathology between subgroups may suggest these factors are specific to certain subsets of ASD symptoms.

2. Material and methods

2.1. Study design

The Finnish Prenatal Study of Autism Spectrum Disorders (FIPS-A) is based on a nested case-control design that relies upon linkages between several nationwide Finnish registries. The sample includes all singleton live births born in Finland between January 1, 1987 and December 31, 2005 ($n=1$ 149 271). These children were followed until December 31, 2007 for the diagnosis of ASD ($n=4713$). A total of 18,849 control subjects were matched from the nationwide medical birth register. The identification of cases and controls, as well as the linkages between several registries is based on a unique identity code, which every Finnish resident has. This identity code remains the same through a person's lifetime. The full description of the study design and data sources is available (Lampi et al., 2011) and will therefore be only summarized herein. The FIPS-A has been authorized by the Ministry of Social Affairs and Health in Finland (STM/2593/2008). The ethics committees of the hospital district of Southwest Finland and the Finnish National Institute for Health and Welfare and the Institutional Review Board of the New York State Psychiatric Institute have given approval for the study.

2.2. National registries

The data were collected from three nationwide registries: the Finnish Hospital Discharge Register (FHDR), the Finnish Medical Birth Register (FMBR) and the Finnish Central Population Register (CPR). The FHDR is maintained by the National Institute of Health and Welfare (THL) and includes all inpatient diagnoses since January 1, 1967 and outpatient diagnoses since January 1, 1998. It contains the personal identity code unique for every person, dates of admission and discharge, primary diagnosis of discharge, and three possible subsidiary diagnoses. It covers all hospitals (somatic, psychiatric, military, prison, private, local health centers) in Finland. FHDR was used to identify ASD cases and parents' psychiatric diagnoses. The diagnostic classification is based on the International Classification of Diseases (ICD). The 8th revision (World Health Organization, 1967) was used from 1969 to 1986, the 9th (World Health Organization, 1977) from 1987 to 1995 and the 10th revision (World Health Organization, 1992) has been used since January 1, 1996. The FMBR is also maintained by THL and includes comprehensive and standardised data on every pregnancy, the prenatal period and the neonatal period up to 7 days on all births in Finland. The FMBR was established in 1987 and it includes the personal identity codes of mothers and every live born child. The FMBR was used to identify the controls and mothers as well as to obtain data on potential confounders as discussed below. The CPR is a computerized national register that contains basic information about Finnish citizens and foreign citizens residing permanently in Finland, including name, personal identity code, address, municipality of residence, citizenship, family relations and date of birth and death. The CPR was used to identify the fathers.

2.3. Case definition

Cases with ASD were identified through the FHDR using ICD-9 (299x) and ICD-10 (F84x) codes. The most recent diagnosis was used in the classification. Therefore there were only 19 cases which had a diagnosis based on ICD-9. No limitations were applied for age at first diagnosis beyond the age attained at the end of follow-up in 2007. Matching criteria assured that cases and matched controls had equivalent follow-up time. We examined the association between parental psychiatric diagnosis and three different subgroups of ASD: childhood autism (F84.0) ($n=1132$), Asperger's syndrome (F84.5) ($n=1785$), and other pervasive developmental disorders/pervasive developmental disorders, unspecified (PDD-NOS) (F84.8/ F84.9) ($n=1796$). The total ASD group combines childhood autism, Asperger's syndrome and PDD-NOS under one category ($n=4713$). In Finland, the diagnosis of ASD is usually made in specialized care units of child neurology, child or adolescent psychiatry or pediatrics. The Finnish register-based diagnosis of childhood autism including children diagnosed after either outpatient or inpatient care alike, has been validated previously (Lampi et al., 2010).

2.4. Control inclusion criteria

All cases were matched to four controls by date of birth (± 30 days), gender, residence in Finland, and place of birth (birth hospital; secondly, regional hospital district if a birth hospital control could not be found). A child is automatically defined to be a resident of Finland if his mother is a citizen of Finland or has a permanent residence permit. Controls were identified through the FMBR and did not meet criteria of ASD or profound/severe intellectual disability according to the FHDR. Overall 18,849 control subjects were matched from the FMBR.

2.5. Maternal and paternal psychiatric disorders

Mothers were identified through the FMBR; fathers from the CPR. Paternity was based on an individual's status as a husband of the mother at the time of the child's birth. If the mother was unmarried, paternity was confirmed by acknowledgment of the father. In this study paternity was established in 98.3% of the subjects, including DNA testing if the father agreed to such testing.

Parents' psychiatric diagnoses from inpatient care were obtained from the FHDR, which includes inpatient diagnoses since January 1, 1967. We included only parents' inpatient care, because there is no information on outpatient diagnoses prior to 1998.

Psychiatric diagnoses were classified into four categories in order of most to least severe. These categories included *schizophrenia spectrum; affective disorders; neurotic and personality disorders and other nonpsychotic disorders (for convenience referred to as anxiety and personality disorders group); alcohol and drug addiction/ abuse (for convenience referred to as substance disorders group)* (see Appendix A). To avoid correlation across diagnoses driven by co-morbidity, parents were assigned to only one diagnostic category. The assignment was based on a hierarchical structure, in the order presented in the preceding sentence; therefore, schizophrenia spectrum disorders were given highest priority and substance disorders the lowest. For example, if the parent had been diagnosed both with severe depression and schizophrenia, she/he was assigned to the schizophrenia spectrum category; a substance disorders diagnosis is interpretable as a diagnosis of substance disorder without history of additional recorded psychiatric diagnosis.

The category of *disorders usually diagnosed in childhood or in adolescence* (*for convenience referred to as childhood disorders*) was examined separately. Therefore a parent diagnosed with disorders in this category (e.g. ASD, attention deficit hyperactivity disorder, oppositional and conduct disorders, learning disabilities, see Appendix A) could also belong to any of the four above-mentioned categories. The separate analysis enables one to isolate the association for childhood- and adolescent-onset psychiatric disorders. Similar systems of classification and hierarchical categorization (Appendix A) have been used in previous studies (Daniels et al., 2008; Larsson et al., 2005).