



Parental psychopathology and offspring attention-deficit/hyperactivity disorder in a nationwide sample



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ABSTRACT

Objective: To study the associations between a wide range of parental psychiatric disorders and offspring attention-deficit/hyperactivity disorder (ADHD).

Method: This study is based on a nested case–control design. The association between parental registered psychiatric diagnoses and offspring ADHD was examined adjusting for socioeconomic and prenatal factors. Data was linked from Finnish nationwide registers. The cases ($n = 10,409$) were all the children born between years 1991 and 2005 in Finland and diagnosed with ADHD by the end of 2011. Four controls without ADHD ($n = 39,124$) were matched for every case by sex, age and place of birth. Main outcomes were adjusted odds ratio (aOR) for parental diagnosis of cases vs controls. Analyses were further stratified by sex. Disorders diagnosed before and after birth were analyzed separately.

Results: The odds ratio for ADHD increased when only mother (aOR 2.2, 95% CI 2.0–2.3), only father (aOR 1.7, 95% CI 1.6–1.8) and both parents (aOR 3.6, 95% CI 3.3–4.0) were diagnosed. Maternal diagnosis showed stronger association than paternal. The weight of association between several parental disorders and offspring ADHD were similar. Maternal psychopathology overall showed stronger associations with girls than boys with ADHD. The diagnoses registered after birth did not show stronger association than the diagnoses registered before. **Conclusions:** Maternal psychopathology showing stronger association than paternal implies that environmental factors or their interaction with genetic factors partly mediates the risk of parental psychopathology. Similar associations between several maternal psychiatric disorders and offspring ADHD points towards the need for investigating some common mother-related risk factors.

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1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is defined as impairment due to inattention, hyperactivity and impulsivity and is estimated to affect 5% of children (Polanczyk et al., 2007). The disorder results from both genetic and environmental risk factors (Tarver et al., 2014). Previous studies that have examined the association between parental psychopathology and ADHD have mostly been based on clinical samples (Margari et al., 2013; Sanchez-Gistau et al., 2015; Segenreich et al., 2015) with rather small sample sizes, selection bias and limited generalizability (Button et al., 2013; Delgado-Rodríguez and Llorca, 2004).

There have only been a few population-based studies that have

examined parental psychopathology and ADHD in their offspring. A study based on Kaiser Permanente in the US showed that the first children born to mothers with ADHD had a five-fold increased risk of ADHD (Musser et al., 2014). Other studies have been based on Swedish register data. A study by Skoglund et al. (2015) showed that parental substance use doubled the risk of offspring to have ADHD, while Larsson et al. (2013) and McCoy et al. (2014) reported that the parents of children with ADHD were twice as likely to have schizophrenia or bipolar disorder than the parents of controls without ADHD. In addition, Lindblad et al. (2011) showed that both the mothers and fathers with children receiving medication for ADHD were two to three times more likely to have psychotic, affective or alcohol disorders.

Despite previous studies demonstrating a number of strong associations between parental psychopathology and offspring ADHD, there are several questions that need to be addressed. First,

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only one previous study included information on both maternal and paternal psychiatric disorders but it included only children who were prescribed ADHD medication (Lindblad et al., 2011). The other studies included either only the mothers or pooled the information on both parents (Larsson et al., 2013; McCoy et al., 2014; Musser et al., 2014; Skoglund et al., 2015). Second, previous studies of parental psychiatric disorders and offspring ADHD have adjusted for limited confounders, which restricts the interpretation of the findings. Larsson et al. (2013) only reported unadjusted results. Skoglund et al. (2015) and Lindblad et al. (2011) adjusted only for socioeconomic factors, such as family income, lone parents or education, while Musser et al. (2014) only adjusted for maternal age, gestational age and child race. McCoy et al. (2014) was the only study that adjusted the results for both socioeconomic and prenatal factors. None of these studies controlled for the other parent's psychiatric morbidity; which is important considering increased non-random mating among people with psychiatric disorders (Nordsletten et al., 2016).

This study contributes to the literature by addressing the limitations of the previous studies, including adjustments for several potential confounders. The main aim was to study the association between a wide range of parental psychiatric disorders and offspring ADHD. Associations between maternal and paternal psychiatric disorders and ADHD, stratified by sex, were studied separately. An additional aim was to study whether parental psychiatric diagnoses that existed before and after child birth had different risk of offspring ADHD.

2. Materials and methods

This is a nationwide register study based on a nested case–control design (Joelsson et al., 2016a). The sampling frame included all 900,603 children born alive between years 1991–2005. Data was linked from three nationwide registers: the Finnish Hospital Discharge Register (FHDR), the Finnish Medical Birth Register and the Finnish Central Population Register. This linkage was achieved by using the personal identity codes that have been assigned to all Finnish citizens and residents. The FHDR contains diagnoses established by Finnish public healthcare specialists and it covers all the inpatient wards in somatic and psychiatric hospitals, local health centers, military wards, prison hospitals and private hospitals. Since 1998, it has also covered the outpatient care provided by public specialized hospitals. In Finland, diagnostic classification is based on the International Classification of Diseases (ICD): ICD-8 between years 1969–1986, ICD-9 between 1987 and 1995 and ICD-10 from 1996 onwards. This register was used to identify cases and obtain data on the psychiatric history of cases, controls and their parents. The Population Register contains basic information on Finnish citizens and permanent residents and it is maintained by the Population Register Centre and local register offices. Individual data recorded in the system includes: a person's name, personal identification code, address, citizenship, family relationships, date of birth and death (if applicable) and emigration/immigration. This register was used to identify the study controls. The Birth Register was established in 1987 and contains standardized data on the perinatal period for all live births and stillbirths with a birth weight of at least 500 g or a gestational age of at least 22 weeks in Finland. Data on prenatal and perinatal factors were obtained from this register and were tested as potential covariates.

Ministry of Social Affairs and Health (STM/1528/2007) and the National Institute of Health and Welfare have authorized the study with ethical approval from the ethics committee of the hospital district of Southwest Finland.

2.1. Study subjects

The cases consisted of all singleton live births in Finland between 1991 and 2005, who were diagnosed with ADHD using the codes F90.X (ICD-10) or 314.X (ICD-9) between the ages of 2–20 years and recorded in the FHDR until 31 December 2011. For every case, four identified controls that were matched by sex, date of birth (± 30 days) and place of birth. The controls had not been diagnosed with ADHD or conduct/oppositional defiant disorder (ICD-10: F91-92, ICD-9: 312). Study subjects with severe or profound intellectual disability (ICD-10: F72-F73, ICD-9: 318), according to the FHDR, were excluded from both the case and controls groups. A total of 10,409 cases and 39,125 controls met the inclusion criteria.

2.2. Parental psychopathology

Parental psychiatric diagnoses were classified into adulthood-onset and childhood-onset disorders. Adulthood-onset disorders included seven categories: schizophrenia and schizoaffective disorders, other psychoses, bipolar disorder, depression, anxiety disorders, personality disorders and substance abuse. If the parent was diagnosed with schizophrenia or a schizoaffective disorder he or she would not be assigned to other adulthood-onset categories. This hierarchical model was applied because schizophrenia and schizoaffective disorders are distinctly severe chronic conditions that cause impairment. In other cases, a parent could be assigned to several diagnostic categories. Childhood-onset disorders included five categories: ADHD, autism spectrum disorders (ASD), conduct disorders, learning and coordination disorders and intellectual disability. The diagnostic codes for each category appear in Table S1, available online.

Parental psychopathology before and after the birth of the child were assessed by studying the onset of the first diagnosis of adulthood-onset disorders. The classification was similar to the one described above, with the exception that schizophrenia, schizoaffective disorders and other psychoses were pooled together as psychotic disorders. Childhood-onset disorders were not studied because their symptoms have been present before child birth by definition.

2.3. Covariates

Factors previously shown to be associated with both offspring ADHD and overall parental psychopathology were selected as covariates in the analyses. The selected covariates were: maternal smoking during pregnancy (Joelsson et al., 2016b; Talati et al., 2013), the parents' ages at the birth of the study child (Chudal et al., 2015; Kessler et al., 1997), the parents' immigrant status (Lehti et al., 2016; Straiton et al., 2014), maternal socioeconomic status (SES) (Larsson et al., 2014; Sareen et al., 2011), previous births (Marín et al., 2014; Patchen and Lanzi, 2013), gestational age (GA) of the study child at birth (Cantarutti et al., 2016; Sucksdorff et al., 2015) and their Apgar score at one minute (Jensen et al., 2013; Sucksdorff et al., 2015). In addition, the results were adjusted with history of other parent's psychopathology. The categorizations of covariates appear in Table S2, available online.

2.4. Statistical analyses

The significance of the association between covariates and parental psychopathology among the controls as well as the association between the covariates and ADHD diagnosis were tested using Pearson's chi-square test. The primary outcome variable was an ADHD diagnosis (yes/no). The exposures were any parental

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