Research Paper

Is the association between offspring intelligence and parents' educational attainment influenced by schizophrenia or mood disorder in parents?

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ABSTRACT

Results from twin, family, and adoption studies all suggest that general intelligence is highly heritable. Several studies have shown lower premorbid intelligence in individuals before the onset of both mood disorders and psychosis, as well as in children and adolescents at genetic high risk for developing schizophrenia. Based on these findings, we aim to investigate if the association between educational achievement in parents and intelligence in their offspring is influenced by schizophrenia or mood disorder in parents. In a large population-based sample of young adult male conscripts (n = 156,531) the presence of a mental disorder in the parents were associated with significantly lower offspring scores on a test of general intelligence, the Børge Priens Prøve (BPP), and higher educational attainment in parents was significantly associated with higher BPP test scores in offspring. A significant interaction suggested that the positive association between maternal education and offspring intelligence was stronger in offspring of mothers with schizophrenia compared to the control group (p = 0.03). The associations between parental education and offspring intelligence are also observed when restricting the sample to conscripts whose parents are diagnosed after 30 years of age. In conclusion, findings from this study show a more positive effect of education on offspring intelligence in mothers with schizophrenia compared to mothers from the control group. This effect could have both environmental and genetic explanations.

1. Introduction

Intelligence is a strong predictor of many important life outcomes, including educational attainment, income, health and lifespan. Results from twin, family and adoption studies all suggests that general intelligence is highly heritable (Benyamin et al., 2014; Deary et al., 2009). Children resemble their parents with respect to intelligence, and current evidence suggests that the effects of family environment on individual differences in children's intelligence decline as the child grows up, while the genetic effects increase (Bouchard and McGue, 1981; McGue et al., 1993; Rutter et al., 1997). One study has shown that heritability increases linearly with age from 41% in childhood and up to 66% in young adulthood (Haworth et al., 2009).

Low intelligence has been shown to be associated with common mental disorders such as mood disorders, personality disorders and alcohol/substance use disorders (Batty et al., 2005; Gale et al., 2010; Mortensen et al., 2005a; Osler et al., 2007b; Urfer-Parnas et al., 2010). A recent study found that a family history of mental disorders was associated with slightly lower cognitive ability (McGrath et al., 2014). A number of studies have focused on the association between intelligence and schizophrenia (Frangou, 2013; Joyce, 2013; Kendler et al., 2015a; Kendler et al., 2015b; Khandaker et al., 2011a; van Scheltinga et al., 2013; Verweij et al., 2013). Intelligence has been found to be impaired in patients with schizophrenia compared to the general population (Kremen et al., 2001) and impaired intelligence is associated with an increased risk of psychosis (Khandaker et al., 2011b). Several birth cohort studies have found that individuals who develop schizophrenia in adulthood achieved lower scores on intelligence tests in childhood

and adolescence than their peers (Welham et al., 2009). Studies have shown lower premorbid intelligence in patients before the onset of psychosis (Urfer-Parnas et al., 2010; Woodberry et al., 2008) as well as in children and adolescents at genetic high risk for developing schizophrenia (Agnew-Blais and Seidman, 2012; Bora et al., 2014; Niemi et al., 2003). For children at high risk for mood disorders, the results are mixed. Overall, the literature suggests that people with mood disorders have lower pre-morbid IQ than controls from the general population (Mortensen et al., 2005b; Urfer-Parnas et al., 2010). The association between unipolar depression and intelligence seems to be stronger than the association between bipolar depression and intelligence (Sørensen et al., 2012) and there is some evidence suggesting that the risk of bipolar disorder could be higher among highly intelligent people (Gale et al., 2013; Higier et al., 2014; MacCabe et al., 2010; Vreeker et al., 2016).

Genetic factors could explain both impaired intelligence and increased risk of schizophrenia in offspring. Bivariate genetic studies (in affected patients and their families) suggest that the phenotypic correlation between cognitive abilities and risk of schizophrenia is substantial and over 90% of their covariance seems to be due to common genetic factors (Touloupoulou et al., 2007). A large-scale population-based study estimated much lower genetic correlations between intelligence and psychosis, indicating that only a small proportion of genetic variance (7%) for psychosis is shared with intelligence (Fowler et al., 2012). Single-nucleotide polymorphism (SNP)-based bivariate analyses may further help to determine robust estimates of the shared genetic underpinnings of both traits. Following these lines, a recent study reported that (a) polygenic risk scores derived to predict increased cognitive ability were associated with a reduced risk of schizophrenia, and conversely that (b) polygenic risk scores for schizophrenia were associated with lower general cognitive ability (Lencz et al., 2014).

Based on the literature, the aim of this study was to evaluate how the association between educational achievement in parents and intelligence in offspring is influenced by mental disorders in the parents. Because we lacked information on parental intelligence, we used parental education as a proxy measure in this study (Mortensen et al., 1989a) and because the analyses included data from a conscription registry, they are based on male offspring only. Thus, the association between parental educational level and offspring intelligence was analyzed in offspring of parents with schizophrenia or mood disorders and in offspring of control parents. We hypothesized that (a) the offspring of parents with mental disorders would have lower intelligence compared to offspring of parents without these mental disorders, and (b) higher educational achievement in parents would be associated with higher intelligence in their offspring. Furthermore, we hypothesized that (c) mental disorders in parents would interfere with the association between educational achievement in parents and offspring intelligence.

2. Material and methods

2.1. Study population

This study was based the on the Danish Conscription Registry (Green, 1996), a nationwide register, which included 183,278 men born in Denmark between 1976 and 1994, who were assessed during the period of time from 2006 until 2012, closest to their 19th birthday. Men with conditions such as severe mental retardation, asthma, and extreme myopia are exempted from conscription (approximately 10–15%), but not all mental health problems are regarded as disqualifying for Danish military service (Osler et al., 2007a; Teasdale, 2009). All Danes are assigned an identification number, which is used as a personal identifier in all Danish national registers, enabling unique linkage of registers. From the Danish Civil Registration System (Pedersen et al., 2006) information on parental age, birth order and multiple pregnancy status was obtained and from Statistics Denmark's

database IDA information on parental education was obtained (Danmarks, 1991). We excluded 21,572 conscripts with parents not born in Denmark, 12 conscripts who had no information on birth order status and 5163 conscripts with admission for any mental disorder prior to their conscription, leaving 156,531 conscripts for the main analyses. Conscripts with the same mother (that is, brothers or maternal half-brothers) comprised a cluster, and allowance for possible within-cluster dependence was made by using robust s.e. estimates provided by the cluster option in Stata.

With respect to mental disorders, we used the ICD10 and ICD8 diagnostic categories (World Health Organization, 1993), based on the admissions recorded in the Danish Psychiatric Central Research Register (Mors et al., 2011). We examined first admission event for two broad diagnostic categories (whatever came first): schizophrenia spectrum disorders (ICD 10: F20–29; ICD8: 295.x, 296.89, 297.x9, 298.29–298.99, 299.04, 299.05, 299.09, 301.83) and mood disorders (ICD 10: F30–39, ICD 8: 296.x9 (excl. 296.89), 298.09, 298.19, 300.49, 301.19).

2.2. Outcome measure

The Børge Priens Prøve (BPP) has been used by the Danish Draft Board since 1956 to assess intelligence in conscripts. The test consists of four subtests; each with about 20 items (78 in total) designed to assess logical, verbal, numerical and spatial reasoning (Teasdale et al., 2011). The test has satisfactory test-retest reliability and a substantial correlation with the Wechsler Adult Intelligence Scale (correlation = 0.82) (Mortensen et al., 1989b). Mean scores on the BPP have changed over recent decades (Teasdale and Owen, 2008). Thus, it is recommended that studies account for year of testing when analyzing the correlates of the BPP score. Higher BPP score indicates higher intelligence.

2.3. Statistical analysis

We estimated mean differences and 95% confidence intervals in BPP test scores according to maternal and paternal education using linear regression in Stata 12 (Stata, College Station, Texas, United States). Year of testing 2006–2012 were categorized in seven categories. The impact of parental education and parental history of admission for mental disorders prior to conscription was examined in a model that adjusted for year of testing, birth order (first, second, third and fourth or later born), and singleton vs multiple birth status. Maternal and paternal education was categorized into five groups (Basic, High School, Vocational, Short duration post-school and Long duration post-school), and basic education was used as the reference category. Additionally, a trend analysis was used to evaluate the linear trend in the association between parental education and BPP test score at conscription. We tested the interaction of the linear trend between maternal and paternal educational level and BPP test score for schizophrenia and mood disorders, respectively, compared to controls. Furthermore, a sensitivity analysis excluding conscripts who had parents with admission for any mental disorder before the age of 30 was conducted because early onset mental disorders may influence the attained education level. All the estimates are reported with 95% confidence intervals.

2.4. Ethics approval

Approval was provided by the Danish Health and Medicines Authority (FSE ID 182) and registered by Danish Data Protection Agency (J.nr. 2012-41-0862).

3. Results

The main analysis was based on 156,531 Danish male conscripts. The mean age of the conscripts at testing was 18.9 years (ranging from