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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

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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 (Toulopoulou 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

Table 1
The table shows the association between mood disorders and schizophrenia spectrum disorders in parents and BPP score at conscription in their male offspring. Controls are used as reference group. n = 156,531.

Cells contains: - n of cases - mean difference [95% CI]		Present in mother			
		Controls	Mood disorders	Schizophrenia spectrum disorders	Row n total
Present in father	Controls	n = 148,712 0 [reference]	n = 3284 –0.51 [−0.84;−0.18]	n = 1084 –0.84 [−1.44;−0.24]	n = 153,080
	Mood disorders	n = 2366 –0.68 [−1.06;−0.29]	n = 99 –2.36 [−4.35;−0.37]	n = 27 –1.99 [−5.40;1.42]	n = 2492
	Schizophrenia spectrum disorders	n = 889 –0.99 [−1.63;0.35]	n = 33 0.14 [−3.38;3.65]	n = 37 1.07 [−2.51;4.66]	n = 959
	Columns n total	n = 151,967	n = 3416	n = 1148	

BPP = Børge Priens Prøve.
The results are adjusted for parental education, birth order, multiple pregnancy status and year of testing.

17 to 31). The overall mean and standard deviation of the BPP cognitive scores was 42.05 (9.46) units (higher scores indicate better cognitive ability).

Table 1 shows adjusted (parental education, birth order, multiple pregnancy status and year of testing) mean difference in BPP test score for male conscripts with 0, 1 and 2 parents with mood disorder or schizophrenia spectrum disorder. We found a relationship between both paternal and maternal disorders and lower mean BPP scores compared with the reference category (controls). For example, compared with the reference category, the male offspring of fathers with schizophrenia spectrum disorders scored 0.99 units lower on the BPP scores (95%CI −1.63 to −0.35). Due to a low number of male offspring with two parents with mental disorders, this subgroup was not analyzed. The reduction in BPP test score in the conscripts was almost similar for paternal and maternal mental disorder. Overall, the presence of a mental disorder in a parent was associated with a significant reduction in BPP test scores in the conscripts.

Table 2 shows adjusted (birth order, multiple pregnancy status and year of testing) mean difference in BPP test score (and 95%CI) for each educational category separately for offspring of a parent with mood disorder, with schizophrenia spectrum disorder, and control, respectively. Irrespective of parental mental health status, higher educational attainment in parents was significantly and substantially associated with higher BPP test scores. For example, offspring of fathers with a long duration post-school education scored between 5.61 and 6.23 units higher on the BPP test scores, compared with the reference category (basic). Excluding conscripts with parents with first admission event for any mental disorder before the age of 30 (n = 5938) in the sensitivity analysis did not change the result essentially (data not shown).

The trend analysis revealed a statistically significant linear trend in the association between parental education and BPP scores. For each educational step, the increase in BPP score was approximately 1.5 units. The trend analysis further showed a significant interaction regarding maternal education in offspring of mothers with schizophrenia compared to offspring of mothers from the control population (p = 0.03). Table 2 shows that the increase in intelligence with higher maternal education seems to be steeper in offspring of mothers with schizophrenia. The sensitivity analysis excluding the 5938 conscripts with parents with first admission event for any mental disorder before the age of 30 showed that conscripts of mothers with schizophrenia spectrum diagnosis scored 2.20 units higher on the BPP test for each educational level (95%CI 1.53 to 2.86). However, conscripts of fathers with schizophrenia scored 1.06 unit higher for each educational level (95%CI 0.42 to 1.71) (data not shown).

Table 2
The table shows the association between parental educational level and offspring BPP score at conscription. Basic education is used as reference group. n = 156,531.

		Schizophrenia spectrum disorder		Mood disorders		Controls	
		n	Mean [95% CI]	n	Mean [95% CI]	n	Mean [95% CI]
Maternal educational level	Basic	459	0 [reference]	1077	0 [reference]	34,064	0 [reference]
	High School	300	2.46 [0.97; 3.96]	1136	2.38 [1.57; 3.19]	59,551	2.30 [2.16; 2.43]
	Vocational	55	5.13 [2.56; 7.70]	153	5.87 [4.32; 7.43]	7135	4.83 [4.61; 5.06]
	Short duration post-school	222	5.74 [4.19; 7.28]	824	4.81 [3.95; 5.66]	40,328	4.67 [4.53; 4.81]
	Long duration post-school	50	8.49 [5.95; 11.02]	137	6.18 [4.36; 8.00]	8494	6.46 [6.23; 6.68]
Trend of maternal educational level			2.00 [1.53; 2.47]		1.57 [1.33; 1.82]		1.47 [1.43; 1.52]
p-Value for test of trend equal the trend in controls		0.03		0.47			
Paternal educational level	Basic	360	0 [reference]	748	0 [reference]	33,242	0 [reference]
	High School	279	2.67 [0.88; 3.83]	901	1.90 [0.96; 2.83]	65,358	1.83 [1.70; 1.96]
	Vocational	48	5.94 [2.58; 9.30]	86	3.84 [1.47; 6.21]	5912	4.64 [4.39; 4.88]
	Short duration post-school	103	4.48 [2.77; 6.19]	401	3.66 [2.58; 4.75]	27,996	4.26 [4.10; 4.41]
	Long duration post-school	49	5.61 [3.59; 7.63]	177	6.23 [4.82; 7.64]	14,015	5.86 [5.67; 6.05]
Trend of paternal educational level			1.53 [1.06; 1.99]		1.35 [1.07; 1.63]		1.40 [1.36; 1.44]
p-Value for test of trend equal the trend in controls		0.60		0.73			

BPP = Børge Priens Prøve.
Missing educational information from 6% of the parents, data not shown.
The results are adjusted for birth order, multiple pregnancy status and year of testing.

4. Discussion

Results from this cohort study of young adult men showed that the presence of a mental disorder in parents was associated with a significant reduction in offspring BPP test scores. This was what we expected to find, based on the literature linking particularly schizophrenia to lower intelligence. Consistent with the existing literature regarding heritability of intelligence, we also found that parental educational achievement was associated with intelligence in the male offspring, regardless of parental mental illness. The trend analysis confirmed that the generally observed relationship between intellectual achievement in parents and children holds true and as parental education increased so too did the level of intelligence in their children. The association of parental education and offspring intelligence was also observed when we restricted the sample to conscripts whose parents were diagnosed after 30 year of age, which maybe could have given the parents the time to take an education. Further, results from this study imply that the association between parents and offspring intelligence seems to be influenced by mental illness in the parents. The significant interaction between mothers with schizophrenia and mothers from the control group suggests that highly educated mothers with schizophrenia appear to confer an intellectual advantage on their sons. This pattern is not observed in highly educated fathers with schizophrenia compared to controls. The sensitivity analysis, which excluded conscripts of parents with any mental disorder before the age of 30, further supports the indication that, the educational level of mothers with schizophrenia has more influence on her child's level of intelligence than the educational level of fathers with schizophrenia.

In a recent study, Anne Ranning and colleagues showed that children living in Denmark with parents with severe mental illness were more likely to live together with their mother with schizophrenia than with their affected father (Ranning et al., 2016). The shared environment with the mother may explain the steeper effect of the mother's versus father's educational attainment. However, it seems reasonable to assume that the shared environment with the mother cannot alone explain the indication that male offspring of mothers with schizophrenia benefitted more from having a higher educated parent than male offspring of mothers from the control group. It can be speculated that women with schizophrenia who are able to become a mother may comprise a better functioning subgroup of women with schizophrenia. The educational level of the mother with schizophrenia could be an indication of a positive environmental effect assuming that the higher educated mother with schizophrenia will have better opportunities for offering her child adequate family conditions compared to an uneducated mother with schizophrenia. Thus, it seems to be of great importance to help and support mothers with schizophrenia to be well educated and so be able to raise their children in supporting and intelligence-stimulating environments.

Another interpretation of the results could be to argue that level of education reflects both cognitive as well as non-cognitive aspects. So, a mother with schizophrenia, who is not as strong on the non-cognitive aspects as a mother without schizophrenia, will therefore need an even higher intelligence to reach the same level of education as a mother without schizophrenia. Following these lines, the stronger effect of education in mothers with schizophrenia observed in this study could therefore be an indication of the association between intelligence in parents and their offspring. This explanation is consistent with the huge amount of studies showing that intelligence is highly heritable. The results could also suggest that the pattern of heritability of intelligence from parents to offspring could be different in families where the mother has schizophrenia. In this study, we were not able to predict any genetic liability for risk of schizophrenia and intelligence, even though the results could point to the possibility of shared genes. A recent genome-wide association study including over 400,000 individuals successfully identified 74 loci associated with educational attainment (Okbay et al., 2016). Notably, the same study also found a positive genetic correlation between educational attainment and risk of schizophrenia using LD score regression, in contrast to a study reporting schizophrenia risk to be associated with low cognition using polygenic risk scores (McIntosh et al., 2013). Future studies including polygenic risk scores and the association between intelligence and schizophrenia may help to shed light on still unanswered questions.

This study was based on a uniquely large population-based sample, and we were able to adjust for potential confounding variables, such as birth order. Despite this strength, this study also has limitations. First, in Denmark, men with certain health conditions are exempted from conscription, thus individuals with some disorders (such as intellectual disability) were under-represented in this sample. Second, our sample consisted of males only, and it is not clear if the same pattern of findings could be observed in female offspring. Third, we did not look at other parental mental disorders. Fourth, we only had information on parent education as a proxy for parental intelligence. Lastly, we did not correct for multiple comparisons.

Due to the methodology used in this study we are not able to differentiate between the relative contribution of the environmental effects or the genetic effects, but results from this study still adds new knowledge that can have important implications for high-risk families. For instance, it might be appropriate to target this group with programs that supports general cognitive abilities and parenting abilities in mothers with schizophrenia.

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Contributors

ANG and LP planned the study, LP analyzed the data, all authors contributed to the interpretation of the results, ANG wrote the manuscript and all authors contributed to finalizing the article.

Conflict of interest

None.

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