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ORIGINAL ARTICLE

The association between family history of mental disorders and general cognitive ability

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There is an emerging literature linking cognitive ability with a wide range of psychiatric disorders. These findings have led to the hypothesis that diminished 'cognitive reserve' is a causal risk factor for psychiatric disorders. However, it is also feasible that a family history of mental disorders may confound this relationship, by contributing to both a slight impairment in cognitive ability, and an increased risk of psychiatric disorder. On the basis of a large, population-based sample of young adult male conscripts ($n = 160\,608$), we examined whether the presence of a family history of a range of mental disorders was associated with cognitive ability, as tested by the Børge Priens Prøve. In those with no individual-level history of mental disorder, a family-level history of a mental disorder was associated with a slight reduction in cognitive ability. In general, this pattern was found regardless of the nature of the psychiatric disorder in the family. Our study suggests that shared familial factors may underpin both cognitive ability and the risk of a wide range of psychiatric disorders. Convergent evidence from epidemiology and genetics suggests that shared genetic factors underpin an unexpectedly diverse range of psychiatric disorders. On the basis of the findings of the current study, we speculate that these same shared genetic factors also contribute to general cognitive ability.

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INTRODUCTION

There is growing interest in the overlap between general cognitive ability and mental disorders. Within the field of schizophrenia research, there is consistent evidence from cross-sectional studies[1] and birth cohorts that a slight reduction in cognitive capacity is associated with an increased risk of psychosis.[2] Indeed, some argue that cognitive deficits are central features of this group of disorders.[3] However, the evidence suggests that cognitive ability may be associated with a much wider spectrum of psychiatric disorders. Apart from the self-evident link between impaired cognitive ability and intellectual handicap, it is widely recognized that many individuals with autism spectrum disorders also have impaired cognitive ability.[4] Population-based studies have confirmed that cognitive ability is associated with common disorders such as depression, personality disorders, adjustment disorder and alcohol/substance use disorders.[5–8] The nonspecificity of the association between intelligence and adult mental disorders has contributed to an overarching theory related to the notion of 'cognitive reserve'.[9] Broadly defined, this theory suggests that reduced general cognitive ability renders the affected individual at increased risk of subsequent neuropsychiatric disorders.[10,11] This model thereby implies that reduced cognitive ability is a *causal risk factor* for psychiatric disorders.

There are several pathways that could link general cognitive ability with the risk of mental illness. From the perspective of neurobiology, a quantitative reduction in critical neuronal components (for example, number of neurons, synaptic properties and so on) may result in a lower threshold beyond which functional impairments break through.[11] In addition, those with suboptimal cognitive reserve may be less able to solve problems and seek help in response to stressful events, which could then amplify their already compromised risk for neuropsychiatric disorders. Conversely, cognitive ability may be compromised as a consequence of the psychiatric disorder. This is especially the case for disorders with a prodromal phase or onset during young adulthood that can disrupt educational achievements.[12,13]

Family-level factors may also influence the relationship between cognitive ability and risk of psychiatric disorder. Genetic factors could underpin both the impaired cognitive ability and the increased risk of mental disorders. In this scenario, the relationship between general cognitive ability and the risk of mental disorders is *confounded* by genetic factors that contribute to both psychiatric and cognitive phenotypes. Evidence to support this hypothesis includes a co-twin-control study, which found that whereas pre-onset cognitive ability was associated with the risk of post-traumatic stress disorder, this relationship could be explained by common genetic factors.[14] If shared heritable factors contribute to both risk of mental disorder and general cognitive ability, then we would predict that (a) the first-degree relatives of individuals with mental disorder should do worse on tests of intelligence and (b) that this association would be identified regardless of mental disorders in the index subjects.

There is a lack of information on the impact of family-level psychiatric history on cognitive ability. We had the opportunity to examine this research question using a large, population-based sample of adult males, who underwent tests of their cognitive ability during assessment for military conscription. On the basis of the literature linking general cognitive ability and a wide range of mental disorders, we hypothesized that otherwise well individuals with first-degree relatives with any mental disorder would have slight reductions in general cognitive ability.

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SUBJECTS AND METHODS

Study population

This study was based on the Danish Conscription Registry,[15] a nationwide register, which included 183 268 men born in Denmark between 1976 and 1994, who were assessed close to their 19th birthday, during the period 2006 and 2011. Men with conditions such as severe mental retardation, asthma and extreme myopia are exempt from conscription (~10–15%); however, not all mental health problems are regarded as disqualifiers for military service.[16,17] All Danish residents are assigned a unique personal identifier in all Danish national registers, enabling unique linkage between registers. Information on parental age, birth order and twin status was obtained from the Danish Civil Registration System.[18] Maternal and obstetric information, such as gestational age and birth weight, was obtained from the Danish Medical Birth Registry.[19] Information on parental education was obtained from the Statistics Denmark's database IDA.[20] We excluded conscripts with one or two foreign-born parents ($n = 22\,658$), as well as those with missing information regarding singleton versus multiple birth status ($n = 2$), leaving 160 608 conscripts for the main analyses.

With respect to psychiatric disorders, we used ICD10 diagnostic categories,[21] based on admission and/or outpatient contact with psychiatric services recorded in the Danish Psychiatric Register.[22] From 1969, the Danish Psychiatric Register contained data on all admissions to Danish psychiatric in-patient facilities, and, from 1995, contained information on all contacts to out-patient psychiatric departments and visits to psychiatric emergency care units. All Danish residents are entitled to free national health care. There are no private psychiatric hospitals in Denmark and all visiting patients are registered in the Danish Psychiatric Central Research Register.

For these analyses, we first examined those who had received a diagnosis for any psychiatric disorder (F00–F99), and then we examined 10 broad diagnostic categories: organic disorders (F00–F09); mental and behavioral disorders due to psychoactive substance abuse (F10–F19); schizophrenia and related disorders (F20–F29); mood disorders (F30–F39); neurotic, stress-related and somatoform disorders (F40–F48); eating disorders (F50); specific personality disorders (F60); mental retardation (F70–F79); pervasive developmental disorders (autism spectrum disorder) (F84); behavioral and emotional disorders with onset usually occurring in childhood and adolescence (which includes attention deficit disorder and conduct disorder; F90–F98). Individuals with a past history of more than one type of disorder were included in each relevant diagnostic category (that is, the case groups are not mutually exclusive).

Outcome measure

The Børge Priens Prøve (BPP) is an intelligence test that has been used by the Danish Draft Board examination since 1956.[16] The test consists of four subtests each with about 20 items (78 in total), designed to assess logical, verbal, numerical and spatial reasoning. The tests are timed and the result is the number of correct answers to the 78 questions (the maximum range for total BPP scores is 0–78). The test has satisfactory test–retest reliability and correlates with both educational achievement and the Wechsler Adult Intelligence Scale (correlation = 0.82).[16,23] The mean differences of 1 unit on the BPP scale correspond approximately to a 1.5-unit difference on the WAIS IQ scale (that is, 10% of the s.d. of this measure). In other words, a drop of 4 units on the BPP test would be approximately equivalent to a drop of 6 units on the WAIS IQ scale. The mean values of the BPP test have changed over recent decades (however, this effect is not linear).[24] Thus, it is recommended that studies account for the year of testing when exploring the correlates of the BPP score.

Statistical analysis

We estimated the mean differences in BPP test scores and 95% confidence intervals using linear regression analysis in Stata 12 (Stata, College Station, TX, USA). Before the main analyses, we examined the association between cognitive ability and psychiatric disorders by examining BPP scores in those with a history of psychiatric disorders before their conscription board examination (that is, affected individuals; individual-level history of psychiatric disorder). For the main analyses we examined the association between a family history of psychiatric disorders versus BPP scores in the subset of men with no past history of psychiatric disorders before their conscription board examination. The impact of individual history of admission for psychiatric disorder before conscription was first examined in a model that only adjusted for year of testing. In a second model, we further adjusted for variables that had previously been associated with BPP scores.[25] These include parental age (in 5-year bands), parental education (on 5 levels), birth order (first, second, third and fourth or later born), singleton versus twin/multiple, small for gestational age (defined as the lowest 10% for a given gestational week) in term-born offspring (that is, gestational age of 37 weeks or later). 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. We reported the estimates with 95% confidence intervals. Finally, we included one *post hoc* analysis based on the subgroup of men with a history of a psychiatric disorder before conscription. We examined whether a positive family history of the disorder of interest was associated with cognitive impairment in this group of affected individuals.

Ethics approval

Approval was provided by the Danish Data Protection Agency. The study was based solely on national and administrative registers and did not require any approval from the ethics committee according to national regulations.

Table 1. Individual-level impact of history of psychiatric disorders before the conscript examination on BPP score (compared with those with no family history of the disorders of interest)

	Number (%) admitted before draft board examination	*Model 1*[a] *Mean (95% CI) difference in BPP scores*	*Model 2*[b] *Mean (95% CI) difference in BPP scores*
F00–F99: any psychiatric history	10 037 (6.2%)	−4.53 (−4.74 to 4.32)	−3.32 (−3.53 to −3.11)
F00–F09: organic (incl. symptomatic) mental disorders	0 (0.0%)	—	—
F10–F19: mental and behavioral disorders due to psychoactive substance abuse	1709 (1.1%)	−7.00 (−7.49 to −6.51)	−5.36 (−5.84 to −4.87)
F20–F29: schizophrenia and related disorders	827 (0.5%)	−3.78 (−4.53 to −3.04)	−2.67 (−3.40 to −1.95)
F30–F39: mood disorders	1646 (1.0%)	−1.79 (−2.27 to −1.31)	−1.20 (−1.66 to −0.74)
F40–F48: neurotic, stress-related, and somatoform disorders	3901 (2.4%)	−3.64 (−3.97 to −3.32)	−2.61 (−2.92 to −2.29)
F50: eating disorders	99 (0.1%)	0.65 (−1.07 to 2.37)	0.34 (−1.38 to 2.07)
F60: specific personality disorders	752 (0.5%)	−3.85 (−4.63 to −3.08)	−2.29 (−3.05 to −1.54)
F70–F79: mental retardation	219 (0.1%)	−18.5 (−19.8 to −17.2)	−15.9 (−17.2 to −14.5)
F84: pervasive developmental disorders (autism spectrum)	635 (0.4%)	−1.39 (−2.19 to −0.59)	−1.44 (−2.23 to −0.64)
F90–F98: behavioral and emotional disorders with onset usually occurring in childhood and adolescence	3776 (2.4%)	−6.10 (−6.43 to −5.76)	−4.45 (−4.78 to −4.11)

Abbreviations: BPP, Børge Priens Prøve; CI, confidence interval. [a]Adjusted for year of testing. [b]Adjusted for year of testing, parental age, parental education, birth order, singleton versus twins and small for gestational age in the 151 104 term-born boys.

Table 2. Number of men with a familial history of psychiatric disorders among the 150 571 without an individual-level history of mental disorders before draft board examination

	Present in mother, n *(%)*	*Present in father,* n *(%)*	*Present in one or more siblings,* n *(%)*
F00–F99: any psychiatric history	10 959 (7.3%)	9719 (6.5%)	16 156 (11.2%)
F00–F09: organic (incl. symptomatic) mental disorders	143 (0.1%)	345 (0.2%)	—
F10–F19: mental and behavioral disorders due to psychoactive substance abuse	1972 (1.3%)	4122 (2.7%)	857 (1.1%)
F20–F29: schizophrenia and related disorders	1110 (0.7%)	965 (0.6%)	601 (0.4%)
F30–F39: mood disorders	4274 (2.8%)	3158 (2.1%)	1882 (1.3%)
F40–F48: neurotic, stress-related and somatoform disorders	6403 (4.3%)	4636 (3.1%)	2521 (1.7%)
F50: eating disorders	317 (0.2%)	12 (0.0%)	458 (0.3%)
F60: specific personality disorders	2668 (1.8%)	2074 (1.4%)	931 (0.6%)
F70–F79: mental retardation	50 (0.0%)	23 (0.0%)	239 (0.2%)
F84: pervasive developmental disorders (autism spectrum)	—	—	304 (0.2%)
F90–F98: behavioral and emotional disorders with onset usually occurring in childhood and adolescence	—	—	1108 (0.8%)

In all, 144 159 patients had at least one sibling, whereas 6412 were only children.

Table 3. Number of men with a familial history of psychiatric disorders among the 10 037 who had an individual-level history of mental disorders before draft board examination

	Present in mother, n *(%)*	*Present in father,* n *(%)*	*Present in one or more siblings,* n *(%)*
F00–F99: any psychiatric history	1833 (18.3)	1391 (13.9)	2282 (23.7)
F00–F09: organic (incl. symptomatic) mental disorders	25 (0.2)	51 (0.5)	—
F10–F19: mental and behavioral disorders due to psychoactive substance abuse	400 (4.0)	675 (6.7)	151 (1.6)
F20–F29: schizophrenia and related disorders	211 (2.1)	158 (1.6)	126 (1.3)
F30–F39: mood disorders	713 (7.1)	390 (3.9)	281 (2.9)
F40–F48: neurotic, stress-related, and somatoform disorders	1144 (11.4)	676 (6.7)	429 (4.5)
F50: eating disorders	51 (0.5)	—	46 (0.5)
F60: specific personality disorders	599 (6.0)	381 (3.8)	165 (1.7)
F70-F79: mental retardation	—	—	46 (0.5)
F84: pervasive developmental disorders (autism spectrum)	—	—	63 (0.7)
F90-F98: behavioral and emotional disorders with onset usually occurring in childhood and adolescence	—	—	228 (2.4)

A total of 9609 had at least one sibling; 428 were only children.

RESULTS

The initial risk set was based on 160 608 Danish male conscripts. At the time of testing their mean BPP score was 42.1 (s.d. 9.5; 95% confidence interval (CI) 42.0–42.1) and the mean age in years was 18.9 (95% CI 18.9–18.9). For those with no history of psychiatric disorders ($n = 150\,571$), the mean BPP score (and 95% CI) was 42.3 (s.d. 9.3; CI 42.3–42.4). For those with a history of psychiatric disorders before conscription ($n = 10\,037$), the mean BPP score (and 95% CI) was 37.9 (s.d. 10.5; CI 37.7–38.2). Table 1 shows the counts of male conscripts with a history of any psychiatric disorder and the nine main disorder groups. The most common groups of disorders before testing were (a) neurotic, stress-related and somatoform disorder ($n = 3901$), (b) mental and behavioural disorders due to psychoactive substance abuse ($n = 1709$) and (c) mood disorders ($n = 1646$). In the adjusted model, all disorders except eating disorders (which were rare in men) were significantly associated with small reductions in BPP scores compared with those with no mental disorders.

Table 2 shows the counts of men with a history of psychiatric disorders in the mother, father or one or more siblings. A small number had both parents affected (for example, mood disorders $n = 494$, substance use $n = 222$). Table 3 shows the comparable counts for the subgroup of men with an individual-level history of psychiatric disorders. Tables 4 and 5 show adjusted mean difference in BPP for those with affected mother, father or at least one sibling, for each of the categories of mental disorders. With few exceptions, the presence of a psychiatric disorder in a family member was significantly associated with slight reductions in BPP scores in the conscripts. The pattern of findings persisted after adjustment for a range of factors; however, there was a reduction in effect size. Unexpectedly, having a sibling with pervasive development disorder was associated with a small but significant increase in BPP score. In those with an individual level history of psychiatric disorders, the presence of a family history of that disorder was also generally associated with a slight drop in BPP scores (however, the estimates were often imprecise and nonsignificant related to the smaller sample size).

DISCUSSION

In a large sample of young adult men, the presence of a family history of a range of psychiatric disorders was significantly associated with a slight reduction in general cognitive ability. Consistent with previous literature, a wide range of psychiatric disorders was associated with lower scores on the BPP, when assessed at the individual level. To our knowledge, we report here for the first time that this association was also found when psychiatric disorders were assessed in parents or siblings of the conscripts. In particular, in those conscripts with no previous psychiatric admission, those with affected family members had significantly lower scores on BPP tests even after adjustment for a

Table 4. Mean differences in BPP test scores and 95% CIs according to familial history of psychiatric disorders (compared with those with no family history of the disorders of interest), adjusted for selected factors (among the 150 571 with no individual-level history of mental disorders before draft board examination)

	Model 1[a] *Mean (95% CI) difference in BPP scores*			*Model 2*[b] *Mean (95% CI) difference in BPP scores*		
	Present in mother	*Present in father*	*Present in one or more siblings*[c]	*Present in mother*	*Present in father*	*Present in one or more siblings*[c]
F00–F99: any psychiatric history	−1.76 (−1.96 to −1.56)	−2.06 (−2.27 to −1.85)	−1.75 (−1.92 to −1.59)	−0.91 (−1.09 to −0.72)	−1.13 (−1.33 to −0.93)	−0.76 (−0.91 to −0.60)
F00–F09: organic (incl. symptomatic) mental disorders	−1.61 (−3.16 to −0.06)	−2.27 (−3.30 to −1.24)	—	−0.44 (−1.91 to 1.04)	−1.29 (−2.27 to −0.32)	—
F10–F19: mental and behavioral disorders due to psychoactive substance abuse	−3.69 (−4.13 to −3.24)	−3.18 (−3.50 to −2.86)	−3.41 (−4.08 to −2.75)	−2.09 (−2.52 to −1.67)	−1.64 (−1.94 to −1.33)	−1.87 (−2.51 to −1.23)
F20–F29: schizophrenia and related disorders	−1.64 (−2.28 to −0.99)	−1.65 (−2.32 to −0.98)	−1.84 (−2.67 to −1.02)	−0.74 (−1.33 to −0.15)	−0.63 (−1.24 to −0.02)	−0.82 (−1.60 to −0.05)
F30–F39: mood disorders	−1.13 (−1.44 to −0.82)	−1.12 (−1.48 to −0.76)	−1.59 (−2.06 to −1.13)	−0.44 (−0.73 to −0.16)	−0.59 (−0.92 to −0.27)	−0.74 (−1.17 to −0.31)
F40–F48: neurotic, stress-related, and somatoform disorders	−2.22 (−2.47 to −1.96)	−2.22 (−2.52 to −1.92)	−1.82 (−2.21 to −1.42)	−1.06 (−1.30 to −0.83)	−1.12 (−1.39 to −0.84)	−0.85 (−1.21 to −0.48)
F50: eating disorders	−0.48 (−1.51 to 0.56)	−0.49 (−4.89 to 3.92)	0.44 (−0.45 to 1.34)	0.40 (−0.59 to 1.38)	−2.33 (−5.84 to 1.17)	0.16 (−0.64 to 0.96)
F60: specific personality disorders	−2.51 (−2.90 to −2.13)	−2.26 (−2.71 to −1.80)	−3.06 (−3.72 to −2.41)	−1.13 (−1.49 to −0.77)	−1.00 (−1.43 to −0.58)	−1.48 (−2.09 to −0.88)
F70–F79: mental retardation	−7.43 (−10.5 to −4.40)	−5.35 (−10.2 to −0.50)	−4.40 (−5.68 to −3.13)	−4.20 (−6.97 to −1.43)	−2.93 (−7.45 to 1.59)	−2.36 (−3.58 to −1.14)
F84: pervasive developmental disorders (autism spectrum)	—	—	0.58 (−0.41 to 1.58)	—	—	1.42 (0.50 to 2.34)
F90–F98: behavioral and emotional disorders with onset usually occurring in childhood and adolescence	—	—	−2.78 (−3.36 to −2.20)	—	—	−1.08 (−1.62 to −0.54)

Abbreviations: BPP, Børge Priens Prøve; CI, confidence interval. In all, 144 159 had at least one sibling, whereas 6412 were only children. [a]Adjusted for year of testing only. [b]Adjusted for year of testing, parental age, parental education, birth order, singleton versus twins, small for gestational age. [c]Compared with others who had at least one sibling (as only children cannot have a sibling with a psychiatric disorder registered).

Table 5. Mean differences in BPP test scores and 95% CIs according to familial history of psychiatric disorders (compared with those with no family history of the disorders of interest), adjusted for selected factors (among the 10 037 with an individual-level history of mental disorders before draft board examination)

	Model 1[a] *Mean (95% CI) difference in BPP scores*			*Model 2*[b] *Mean (95% CI) difference in BPP scores*		
	Present in mother	*Present in father*	*Present in one or more siblings*[c]	*Present in mother*	*Present in father*	*Present in one or more siblings*[c]
F00–F99: any psychiatric history	−0.97 (−1.51 to −0.43)	−2.35 (−2.95 to −1.75)	−1.33 (−1.84 to −0.83)	−0.19 (−0.71 to 0.34)	−1.30 (−1.88 to −0.73)	−0.19 (−0.68 to 0.30)
F00–F09: organic (incl. symptomatic) mental disorders	−1.80 (−6.28 to 2.69)	−2.59 (−5.36 to 0.18)	—	0.02 (−4.28 to 4.32)	−0.68 (−3.31 to 1.96)	—
F10–F19: mental and behavioral disorders due to psychoactive substance abuse	−2.78 (−3.80 to −1.75)	−3.19 (−4.01 to −2.38)	−3.86 (−5.56 to −2.16)	−1.61 (−2.59 to −0.62)	−1.66 (−2.45 to −0.88)	−2.62 (−4.21 to −1.02)
F20–F29: schizophrenia and related disorders	−0.36 (−1.80 to 1.07)	−1.41 (−3.02 to 0.20)	−1.87 (−3.82 to 0.08)	0.14 (−1.25 to 1.53)	−0.22 (−1.77 to 1.33)	−0.65 (−2.49 to 1.20)
F30–F39: mood disorders	−0.59 (−1.40 to 0.23)	−1.67 (−2.67 to −0.68)	−1.42 (−2.75 to −0.09)	0.08 (−0.69 to 0.85)	−0.94 (−1.90 to 0.01)	−0.50 (−1.73 to 0.73)
F40–F48: neurotic, stress-related and somatoform disorders	−1.23 (−1.88 to −0.58)	−2.25 (−3.08 to −1.42)	−1.18 (−2.22 to −0.14)	−0.28 (−0.90 to 0.35)	−1.01 (−1.81 to −0.22)	−0.14 (−1.12 to 0.83)
F50: eating disorders	−0.95 (−3.91 to 2.01)	—	−0.78 (−4.05 to 2.48)	−0.62 (−3.55 to 2.31)	—	−0.35 (−3.31 to 2.61)
F60: specific personality disorders	−1.19 (−2.06 to −0.33)	−2.67 (−3.77 to −1.56)	−2.33 (−4.15 to −0.51)	−0.21 (−1.04 to 0.62)	−1.16 (−2.25 to −0.07)	−1.04 (−2.75 to 0.67)
F70–F79: mental retardation	—	—	−5.84 (−9.44 to −2.24)	—	—	−3.35 (−6.68 to −0.02)
F84: pervasive developmental disorders (autism spectrum)	—	—	0.30 (−2.19 to 2.79)	—	—	0.57 (−1.89 to 3.03)
F90–F98: behavioral and emotional disorders with onset usually occurring in childhood and adolescence	—	—	−1.95 (−3.41 to −0.50)	—	—	−0.67 (−2.03 to 0.69)

Abbreviations: BPP, Børge Priens Prøve; CI, confidence interval. In all, 9609 had at least one sibling; 428 were only children. [a]Adjusted for year of testing only. [b]Adjusted for year of testing, parental age, parental education, birth order, singleton vs twins, small for gestational age. [c]Compared with others who had at least one sibling (as only children cannot have a sibling with a psychiatric disorder registered).

range of covariates. The nature of the relationship (mother, father or sibling) did not substantially alter the pattern of the relationship. This general pattern was confirmed for most categories of psychiatric disorders, including (a) schizophrenia, (b) mental and behavioural disorders due to psychoactive disorders, (c) mood disorders and (d) neurotic, stress-related and somatoform disorders. In the adjusted models, the presence of a family history of any psychiatric disorder was associated with a small but significant drop in BPP scores (the equivalent of less than 1.7 WAIS IQ units). In the subgroup of men with a past history of psychiatric disorders, having affected family members with the same disorders of interest was generally associated with numerical reductions in cognitive ability also. We stress that these group differences are slight and unlikely to result in functional impairment or disruptions to academic or vocational outcomes.

Our findings suggest that shared familial factors (that is, genetic and/or shared environmental factors), associated with psychiatric illness have an impact on cognitive ability in young adult men. Hypotheses that implicate impaired cognitive reserve as a causal factor for psychiatric disorder may not reflect the complex nature of the relationship. Just as shortness of breath does not 'cause' cardiac failure, impaired cognitive ability may not 'cause' mental disorders. Both phenotypes may be the consequence of a prior neurobiological process.

Recent epidemiological studies indicate that the presence of a family history of a wide range of common psychiatric disorders is associated with an increased risk of schizophrenia.[26] We speculate that genetic factors associated with a range of mental disorders may also be associated with slight changes in cognitive ability. However, shared environmental factors may also confound and moderate the relationship between the variables of interest. For instance, the presence of a mental disorder in a family member is often disruptive for the entire family, in that it can trigger a cascade of social disadvantage that may be reflected in academic achievements of unaffected family members. Thus, complex gene–environment correlations may influence the association between the variables of interest.

Limitations of the study

The study has several important limitations. In Denmark, men with certain health conditions are exempt from conscription; thus, individuals with some disorders (such as intellectual disability) were under-represented. Thus, our sample may have been systematically biased—those with severe mental illness would be under-represented in this sample. In addition, our sample consisted of young males only, and it is not clear whether the same pattern of findings would be found in females, or in older men (some men may develop incident mental disorders after conscription). Furthermore, we had only one composite measure of general cognitive ability measured at one time point, whereas it is known that the relative influence of genetic versus nongenetic factors on cognitive ability changes across the lifespan.[27] Whereas the Danish Psychiatric Register covered those in contact with inpatient and outpatient services, it does not include individuals who have only received care from their general practitioner (thus, common disorders such as depression and anxiety would be under-represented in this study). Lastly, although we had information on parental education, we were not able to control general cognitive ability in the family member. Despite these factors, our study is based on a large sample and was able to adjust for a wide range of potential confounding variables, including parental education.

Implications for future research

Twin-based studies have suggested substantial shared genetic variance between psychosis and intelligence.[28–30] However, as we learn more about the polygenic architecture of intelligence and

mental disorders, single-nucleotide length polymorphism (SNP)-based bivariate analyses may provide more robust estimates of the shared genetic contribution of common genetic variants.[31–33] Indeed, a recent study reported that (a) polygenic SNP scores derived to predict increased cognitive ability were associated with a reduced risk of schizophrenia, and conversely that (b) polygenic SNP scores derived to predict increased risk of schizophrenia were associated with lower scores on cognitive ability.[34]

On the basis of the convergent evidence from epidemiology[26] and genetics,[35] there is a growing consensus that shared genetic factors underpin an unexpectedly diverse range of psychiatric disorders. On the basis of the results of the current study, and in light of the recent cross-disorder polygene score studies,[34] we speculate that these same shared genetic factors may also contribute to general cognitive ability. This hypothesis should be testable as sample sizes grow, and polygene risk profile scores for psychiatric disorders and intelligence acquire greater predictive value. Bivariate analyses of SNP-based heritability between these traits may provide additional clues to the nature of the relationship. Future hypotheses that link cognitive reserve and risk of psychiatric disorder should take into account family-level factors.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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