

Supplementary Material

Adolescent residential mobility, genetic liability, and risk of schizophrenia, bipolar disorder, and major depression

Diana Paksarian, Betina B Trabjerg, Kathleen R. Merikangas, Ole Mors, Anders D. Børghlum, David M. Hougaard, Merete Nordentoft, Thomas Werge, Carsten B. Pedersen, Preben B. Mortensen, Esben Agerbo, Henriette Thisted Horsdal

Contents:

Table S1: Characteristics of cases of schizophrenia, bipolar disorder, and major depression, and of the random population subcohort, in a prospective case-cohort study

Table S2: Associations between genetic liability for schizophrenia, bipolar disorder, and major depression, and residential mobility from ages 10 through 14 among the random population subcohort, restricting to those whose parents were both born in Denmark

Table S3: Associations of residential mobility from ages 10 through 14 with schizophrenia, bipolar disorder, and major depressive disorder, under various adjustments, restricting to those whose parents were both born in Denmark

Table S4: Associations between genetic liability for schizophrenia, bipolar disorder, and major depression, and residential mobility from ages 10 through 14 among individuals in the random population subcohort, treating mobility as a continuous variable

Table S5: Associations of residential mobility from ages 10 through 14 with schizophrenia, bipolar disorder, and major depressive disorder, under various adjustments, treating mobility as a continuous variable

Figure: Mean polygenic risk score for schizophrenia, bipolar disorder, and major depressive disorder (MDD) according to the number of changes of municipality from ages 10 through 14 among individuals in the random population subcohort, restricting to those whose parents were both born in Denmark

Table S1: Characteristics of cases of schizophrenia, bipolar disorder, and major depression, and of the random population subcohort, in a prospective case-cohort study

Characteristic	Schizophrenia cases (n=4,207) N (%)	Bipolar disorder cases (n=1,402) N (%)	Major depression cases (n=18,215) N (%)	Subcohort (n=17,582) N (%)
Residential mobility from ages 10 through 14				
0 moves	3,457 (82.17)	1,180 (84.17)	15,481 (84.99)	15,965 (90.80)
1 move	474 (11.27)	141 (10.06)	1,825 (10.02)	1,181 (6.72)
2 moves	178 (4.23)	52 (3.71)	594 (3.26)	322 (1.83)
3+ moves	98 (2.33)	29 (2.07)	315 (1.73)	114 (0.65)
Sex				
Male	2,402 (57.10)	540 (38.52)	5,576 (30.61)	8,948 (50.89)
Female	1,805 (42.90)	862 (61.48)	12,639 (69.39)	8,634 (49.11)
Polygenic Risk Score (mean, SD)	0.29 (1.07)	0.28 (1.02)	0.25 (0.98)	0.00 (1.00)
Parental history of mental disorder				
Broad schizophrenia	95 (2.26)	39 (2.78)	239 (1.31)	120 (0.68)
Affective disorder	29 (0.69)	20 (1.43)	109 (0.60)	67 (0.38)
Other disorder	245 (5.82)	67 (4.78)	848 (4.66)	505 (2.87)
None	3,838 (91.23)	1,276 (91.01)	17,019 (93.43)	16,890 (96.06)
Parental place of birth				
Both born in Denmark	3,521 (83.69)	1,227 (87.52)	16,346 (89.74)	15,430 (87.76)
One born in Denmark	435 (10.34)	118 (8.42)	1,479 (8.12)	1,280 (7.28)
Neither born in Denmark	251 (5.97)	57 (4.07)	390 (2.14)	872 (4.96)
Paternal age				
<= 20 years	134 (3.19)	38 (2.71)	494 (2.71)	274 (1.56)
21-25 years	861 (20.47)	256 (18.26)	3,595 (19.74)	2,775 (15.78)
26-30 years	1,440 (34.23)	481 (34.31)	6,358 (34.91)	6,369 (36.22)
31-35 years	1,000 (23.77)	377 (26.89)	4,615 (25.34)	5,044 (28.69)
36-40 years	510 (12.12)	174 (12.41)	2,142 (11.76)	2,166 (12.32)
>= 41 years	262 (6.23)	76 (5.42)	1,011 (5.55)	954 (5.43)
Urbanicity				
Capital	600 (14.26)	181 (12.91)	2,030 (11.14)	2,035 (11.57)
Capital suburb	656 (15.59)	174 (12.41)	2,564 (14.08)	2,428 (13.81)
Provincial city	466 (11.08)	226 (16.12)	2,127 (11.68)	2,099 (11.94)
Provincial town	1,159 (27.55)	378 (26.96)	5,289 (29.04)	4,906 (27.90)
Rural	1,326 (31.52)	443 (31.60)	6,205 (34.07)	6,114 (34.77)
Maternal education				
Primary education	2,047 (48.66)	590 (42.08)	8,389 (46.06)	6,115 (34.78)
Higher than primary	1,835 (43.62)	730 (52.07)	8,921 (48.98)	10,687 (60.78)

Missing	325 (7.73)	82 (5.85)	905 (4.97)	780 (4.44)
Paternal employment				
Outside workforce	940 (22.34)	234 (16.69)	2,817 (15.47)	2,374 (13.50)
In workforce	3,239 (76.99)	1,161 (82.81)	15,319 (84.10)	15,142 (86.12)
Missing	28 (0.67)	7 (0.50)	79 (0.43)	66 (0.38)
Living with both parents at age 10				
No	1,818 (43.21)	569 (40.58)	6,966 (38.24)	4,751 (27.02)
Yes	2,389 (56.79)	833 (59.42)	11,249 (61.76)	12,831 (72.98)
Birth year				
1991-1985	1,470 (34.94)	518 (36.95)	6,534 (35.87)	4,016 (22.84)
1986-1989	1,482 (35.23)	495 (35.31)	5,832 (32.02)	4,062 (23.10)
1990-1993	1,052 (25.01)	318 (22.68)	4,479 (24.59)	4,606 (26.20)
1994-1997	203 (4.83)	71 (5.06)	1,370 (7.52)	4,898 (27.86)

Note: Paternal age, urbanicity, maternal education, and paternal employment were measured at birth. All 3 polygenic risk scores were standardized in the subcohort to have mean of 0.00 and standard deviation of 1.00; subcohort sizes were slightly smaller for calculation of schizophrenia PRS (n=17,579) and major depression PRS (n=17,481).

Table S2: Associations between genetic liability for schizophrenia, bipolar disorder, and major depression, and residential mobility from ages 10 through 14 among individuals in the random population subcohort, restricting to those whose parents were both born in Denmark

	One Move OR (95% CI)	Two Moves OR (95% CI)	Three + Moves OR (95% CI)
Schizophrenia PRS	1.05 (0.99 - 1.12)	0.98 (0.87 - 1.10)	1.17 (0.96 - 1.43)
Bipolar Disorder PRS	1.02 (0.96 - 1.09)	1.08 (0.96 - 1.22)	0.97 (0.79 - 1.18)
Major Depression PRS	1.09 (1.02 - 1.16)	1.08 (0.96 - 1.22)	1.17 (0.96 - 1.43)
Parental history of mental disorder	2.28 (1.78 - 2.92)	2.52 (1.63 - 3.90)	3.14 (1.62 - 6.08)

Note: PRS = polygenic risk score. PRS estimates are adjusted for ancestry using the first 10 principal components. Subcohort sizes were n=15,430 for schizophrenia and bipolar disorder and n=15,372 for major depression.

Table S3: Associations of residential mobility from ages 10 through 14 with schizophrenia, bipolar disorder, and major depressive disorder, under various adjustments, restricting to those whose parents were both born in Denmark

		Model 1^a	Model 2^b	Model 3^c	Model 4^d
Outcome	Moves	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Schizophrenia	0	Ref.	Ref.	Ref.	Ref.
	1	1.89 (1.67-2.15)	1.83 (1.61-2.08)	1.76 (1.54-2.01)	1.43 (1.24-1.65)
	2	2.93 (2.36-3.63)	2.87 (2.31-3.57)	2.75 (2.20-3.43)	1.97 (1.56-2.49)
	3+	4.28 (3.08-5.95)	4.08 (2.91-5.73)	3.60 (2.50-5.19)	2.46 (1.71-3.54)
Bipolar disorder	0	Ref.	Ref.	Ref.	Ref.
	1	1.64 (1.34-2.00)	1.61 (1.31-1.97)	1.55 (1.26-1.91)	1.36 (1.09-1.70)
	2	2.23 (1.58-3.14)	2.11 (1.49-2.99)	2.07 (1.46-2.94)	1.77 (1.23-2.54)
	3+	4.93 (3.11-7.81)	4.79 (2.98-7.68)	4.27 (2.63-6.93)	3.20 (1.93-5.31)
Major depressive disorder (MDD)	0	Ref.	Ref.	Ref.	Ref.
	1	1.59 (1.45-1.75)	1.55 (1.41-1.71)	1.53 (1.39-1.69)	1.33 (1.20-1.47)
	2	2.04 (1.72-2.42)	1.95 (1.63-2.33)	1.91 (1.60-2.29)	1.50 (1.25-1.81)
	3+	3.50 (2.66-4.62)	3.24 (2.44-4.31)	3.07 (2.28-4.14)	2.42 (1.81-3.25)

^a Adjusted for age, sex, and birth year

^b Model 1, plus adjustment for the polygenic risk score and ancestry

^c Model 2, plus adjustment for family history of any mental disorder

^d Model 4, plus adjustment for urbanicity, paternal age, parental SES, parental place of birth, and family structure at age 10

Note: There were 3,521 schizophrenia cases, 1,227 bipolar disorder cases, 16,346 MDD cases, and 15,430 in the random population subcohort (15,427 for analysis of schizophrenia, and 15,339 for analysis of MDD)

Table S4: Associations between genetic liability for schizophrenia, bipolar disorder, and major depression, and residential mobility from ages 10 through 14 among individuals in the random population subcohort, treating mobility as a continuous variable

	β (95% CI)
Schizophrenia PRS	0.007 (-0.002 - 0.015)
Bipolar Disorder PRS	0.002 (-0.005 - 0.010)
Major Depression PRS	0.011 (0.004 - 0.018)
Parental history of mental disorder	0.132 (0.098 - 0.166)

Note: PRS = polygenic risk score. PRS estimates are adjusted for ancestry using the first 10 principal components. Subcohort sizes were n=17,582 for schizophrenia and bipolar disorder and n=17,517 for major depression.

Table S5: Associations of residential mobility from ages 10 through 14 with schizophrenia, bipolar disorder, and major depressive disorder, under various adjustments, treating mobility as a continuous variable

	Model 1^a	Model 2^b	Model 3^c	Model 4^d
Outcome	HRs (95% CI)	HRs (95% CI)	HRs (95% CI)	HRs (95% CI)
Schizophrenia	1.59 (1.50-1.69)	1.56 (1.47-1.66)	1.52 (1.43-1.63)	1.34 (1.25-1.43)
Bipolar disorder	1.51 (1.38-1.64)	1.50 (1.37-1.64)	1.46 (1.33-1.60)	1.34 (1.22-1.48)
Major depression	1.44 (1.37-1.51)	1.41 (1.34-1.48)	1.39 (1.31-1.46)	1.26 (1.19-1.33)

^a Adjusted for (age), sex, and birth year.

^b Model 1, plus adjustment for the polygenic risk score and ancestry.

^c Model 2, plus adjustment for family history of any mental disorder.

^d Model 3, plus adjustment for urbanicity, paternal age, parental SES, parental place of birth, and family structure at age 10.

Note: There were 4,207 schizophrenia cases, 1,402 bipolar disorder cases, 18,215 MDD cases, and 17,582 in the random population subcohort (17,579 for analysis of schizophrenia and 17,481 for analysis of MDD)

Figure: Mean polygenic risk score (PRS) for schizophrenia, bipolar disorder, and major depressive disorder (MDD) according to the number of changes of municipality from ages 10 through 14 among individuals in the random population subcohort, restricting to those whose parents were both born in Denmark (n=15,430 (15,372 for MDD)). Polygenic scores are adjusted for ancestry using the first 10 principal components.

