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Environment risk factors have different impact on bipolar and psychotic disorders: an analysis of MHGP survey

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Dear Editor

Dykxhoorn *et al.* (2018) recently analysed the Swedish registers and calculated the incidence of (i) affective and non-affective psychotic disorders and (ii) non-psychotic bipolar disorder, according to migrant status among residents born between 1982 and 1996. They found that all psychotic disorders were significantly elevated among first- and second-generation migrants (1GM and 2GM), including schizophrenia and schizoaffective disorders, affective psychotic disorder and other non-affective psychotic disorders. Moreover, the incidence of non-psychotic bipolar disorder was significantly reduced among 1GM and non-significantly different among 2GM. Authors concluded to a specific effect of the migrant-related exposures on the risk of psychotic disorders as no effects were observed for non-psychotic bipolar disorders.

We read with interest this study that adds to the literature highlighting continuities and discontinuities between psychotic and bipolar disorders. Based on clinical overlaps and multi-scale similarities, some authors have argued for going beyond the Kraepelinian dichotomy and for pooling in a single entity these two diagnoses of psychotic and bipolar disorders (Guloksuz and van Os, 2018). Interestingly, several studies have suggested the involvement of partially shared and partially different environmental exposures between these disorders (Demjaha *et al.*, 2012).

To disentangle these shared and specific environmental risk factors, studies that focus on different risk factors and different disorders are required. Moreover, these studies should also consider separately psychotic bipolar disorders, i.e. a phenotype considered as intermediate between non-psychotic bipolar disorder and psychotic disorder. Mental Health in General Population (MHGP) survey offers such an opportunity. Moreover, it allows for the first time to study the third-generation of migrants (3GM). Thus, the aim of the present study was to compare the influence of different environment risk factors [migrant status, history of trauma, substance use disorders (SUDs) and alcohol use disorders (AUDs)] on the prevalence of psychotic disorders, and of psychotic and non-psychotic bipolar disorder in the MHGP survey.

The MHGP survey, conducted by the World Health Organization Collaborating Centre, interviewed 38 694 subjects selected by a quota sampling method in France between 1999 and 2003 (47 sites). For each subject, the *Mini International Neuropsychiatric Interview* (MINI) was used to screen for 10th International Classification of Diseases defined psychiatric disorders in the general population. To define bipolar disorders with and without psychotic symptoms, the seven psychotic symptoms of the psychotic disorders section were used. Further details on MHGP survey and diagnoses procedures are available elsewhere (Amad *et al.*, 2013; Pignon *et al.*, 2017, 2018).

To compare specifically subjects with psychotic disorders to those with bipolar disorders, subjects with both diagnoses were excluded. Four groups were defined: psychotic disorders, bipolar disorders with psychotic symptoms (i.e. psychotic bipolar disorders), non-psychotic bipolar disorders and 'control' subjects without psychotic or bipolar disorders. We performed logistic regression analyses to compare the different risk factors between the four groups, defining the control group as reference. We controlled these analyses for age, sex, and educational, income and marital status. All statistical analyses were performed using R software version 3.1.0 (http://www.R-project.org).

Of the 38 694 individuals interviewed, 140 subjects were excluded because of dual diagnoses of bipolar and psychotic disorders (0.36% of the total sample). At the end, 474 subjects with bipolar disorders, including 293 without psychotic symptoms (0.76%) and 181 with psychotic symptoms (0.47%), and 933 subjects with psychotic disorders (2.42%) were analysed.

Table 1. Logistic regression analyses* to compare subjects with psychotic and non-psychotic bipolar disorder, and psychotic disorders, to subjects without bipolar or psychotic disorder

	Controls (*n* = 37 147) (reference)		Non-psychotic bipolar disorder (*n* = 293)						Psychotic bipolar disorder (*n* = 181)						Psychotic disorder (*n* = 933)					
	N	%	*N*	%	OR	95% CI −	95% CI +	*p*	*N*	%	OR	95% CI−	95% CI +	*p*	*N*	%	OR	95% CI−	95% CI +	*p*
Age band																				
18–29 years	9216	24.8	114	38.9	**3.76**	**2.10**	**6.75**	**<0.001**	46	25.4	1.80	0.95	3.40	0.072	298	31.9	**1.44**	**1.09**	**1.92**	**0.011**
30–44 years	10 578	28.5	108	36.9	**3.93**	**2.28**	**6.77**	**0.002**	72	39.8	**2.53**	**1.46**	**4.38**	**<0.001**	302	32.4	**1.82**	**1.41**	**2.35**	**<0.001**
45–59 years	8121	21.9	48	16.4	**2.40**	**1.37**	**4.23**	**0.002**	35	19.3	1.52	0.86	2.69	0.153	191	20.5	**1.77**	**1.37**	**2.29**	**<0.001**
60+years (reference)	9232	24.9	23	7.8	–	–	–	–	28	15.5	–	–	–	–	142	15.2	–	–	–	–
Gender																				
Male (reference)	17 057	45.9	172	58.7	–	–	–	–	106	58.6	–	–	–	–	470	50.4	–	–	–	–
Female	20 090	54.1	121	41.3	0.80	0.62	1.03	0.372	75	41.4	0.75	0.55	1.03	0.073	463	49.6	1.08	0.94	1.25	0.255
Education level																				
No education – elementary level	8959	24.1	49	16.7	1.21	0.80	1.83	0.372	42	23.2	**1.70**	**1.03**	**2.80**	**0.037**	192	20.6	1.10	0.88	1.39	0.406
Secondary level	18 177	48.9	170	58	1.15	0.86	1.53	0.349	97	53.6	1.31	0.89	1.92	0.164	505	54.1	1.10	0.93	1.30	0.43
University level (reference)	10 011	26.9	74	25.3	–	–	–	–	42	23.2	–	–	–	–	236	25.3	–	–	–	–
Marital status																				
Married (reference)	20 322	55.2	112	38.2	–	–	–	–	79	43.9	–	–	–	–	348	37.5	–	–	–	–
Never married	10 120	27.5	126	43	1.25	0.92	1.72	0.159	62	34.4	**1.55**	**1.03**	**2.33**	**0.036**	402	43.3	**1.75**	**1.46**	**2.09**	**<0.001**
Separated	2971	8.1	48	16.4	**2.43**	**1.69**	**3.50**	**<0.001**	27	15.0	**2.22**	**1.40**	**3.55**	**<0.001**	118	12.7	**1.75**	**1.40**	**2.19**	**<0.001**
Widowed	3430	9.3	7	2.4	0.76	0.32	1.77	0.520	12	6.7	1.57	0.77	3.20	0.212	61	6.6	1.21	0.87	1.67	0.258
Income level[a]																				
Low	13 685	37.9	145	51.2	1.59	1.10	2.29	0.012	68	38.0	0.79	0.50	1.24	0.298	482	53.4	1.63	1.32	2.01	<0.001
Medium	14 589	40.4	93	32.9	1.05	0.73	1.25	0.777	75	41.9	0.94	0.62	1.42	0.760	279	30.9	1.02	0.82	1.25	0.908
High (reference)	7846	21.7	45	15.9	–	–	–	–	36	20.1	–	–	–	–	141	15.6	–	–	–	–
Migrant status																				
Native (reference)[b]	27 722	74.6	200	68.3	–	–	–	–	135	74.6	–	–	–	–	593	63.6	–	–	–	–
1GM	1943	5.2	16	5.5	0.93	0.55	1.59	0.793	14	7.7	1.41	0.80	2.46	0.232	75	8.0	**1.62**	**1.26**	**2.08**	**<0.001**
2GM	3944	10.6	39	13.3	0.88	0.61	1.27	0.491	16	8.8	0.70	0.41	1.18	0.181	131	14.0	**1.24**	**1.02**	**1.52**	**0.032**
3GM	3538	9.5	38	13	1.02	0.71	1.46	0.908	16	8.8	0.78	0.46	1.32	0.350	134	14.4	**1.43**	**1.17**	**1.74**	**<0.001**

History of trauma																			
Yes	10 637	28.7	147	50.2	**2.15**	**1.69**	**2.74**	**<0.001**	68	37.8	**1.41**	**1.03**	**1.92**	**0.030**	474	49.2	**2.33**	**2.04**	**2.67**	**<0.001**
No (reference)	26 742	71.3	146	48.8	-	-	-	-	112	62.2	-	-	-	-	459	50.8	-	-	-	-
Alcohol use disorders																				
Yes	1452	3.8	50	17.1	**2.17**	**1.53**	**3.08**	**<0.001**	30	16.6	**3.47**	**2.24**	**5.36**	**<0.001**	121	13.0	**2.03**	**1.62**	**2.55**	**<0.001**
No (reference)	35 695	96.1	243	82.9	-	-	-	-	151	83.4	-	-	-	-	812	87.0	-	-	-	-
Substance use disorders																				
Yes	866	2.3	51	17.4	**3.90**	**2.70**	**5.62**	**<0.001**	10	5.5	1.25	0.63	2.50	0.520	104	11.1	**2.58**	**2.01**	**3.33**	**<0.001**
No (reference)	36 281	97.7	242	82.6	-	-	-	-	171	94.5	-	-	-	-	829	88.9	-	-	-	-

1GM, 2GM and 3GM: first-, second- and third-generation of migrants; 95% CI− and 95% CI+: 95% confidence interval lower and upper limits; OR: odds ratio; *p*: *p*-value.
In bold: the significant ($p < 0.05$) relationships.
[a]Monthly income levels: low <€1.650/household; medium: €1.650–€3.200/household; high: >€3.200/household.
[b]Subject who was born in and whose parents and grandparents were born in metropolitan France.
*Analyses adjusted for age, sex, and educational, income and marital status.

Table 1 shows sociodemographic and clinical characteristics of the four groups. The rates of migrants (1GM, 2GM and 3GM) were higher among subjects with psychotic disorders (ORs between 1.52 and 2.08), in contrast to the rates of migrants in psychotic and non-psychotic bipolar disorders groups. Rates of subjects with a history of trauma were higher in the three groups (ORs between 1.41 and 2.33). Likewise, for AUDs (ORs between 2.03 and 3.47). The rates of subjects with SUDs were higher among the subjects with non-psychotic bipolar disorders (OR = 3.90) and among subjects with psychotic disorders (OR = 2.58).

These results confirm the Demjaha *et al.* (2012) observation suggesting that, between bipolar and psychotic disorders, environment exposures involved are partially shared and partially different. Our results are also consistent with Dykxhoorn *et al.*'s study on the different effects of migrant-related exposures on the two types of disorders: 1GM and 2GM status were associated with increased incidence of psychotic disorders and not with non-psychotic bipolar disorders. However, unlike Dykxhoorn *et al.*, we did not find any association between migrant status and the frequency of psychotic bipolar disorders. Interestingly, a recent meta-analysis of six studies considering the risk of mood disorder among migrants did not find any association between 1GM status and bipolar disorder (Mindlis and Boffetta, 2017). Our study also presents data concerning 3GM, also showing increased rates of psychotic disorders but not bipolar disorders, including those with psychotic symptoms, among migrants.

The history of trauma has been widely studied in the scientific literature that shows an increased risk associated with both psychotic and bipolar disorders (Carr *et al.*, 2013), as found in our study. Finally, we did not find different impact of either AUDs or SUDs on psychotic or bipolar disorders prevalences. This is in line with actual knowledge of an increased risk for both disorders regarding SUDs that could represent an unspecific risk factor of both bipolar and psychotic disorders (Demjaha *et al.*, 2012).

Of note, several other environment factors are known to have a different impact on bipolar and psychotic disorders. Urbanicity, one of the oldest and best acknowledged risk factor of psychotic disorders (March *et al.*, 2008), has a slight or null effect on the risk of bipolar disorder (Mortensen *et al.*, 2003). Studies of urban neighbourhood variations of incidence and prevalence also showed different patterns for affective and non-affective psychotic disorders (March *et al.*, 2008). Obstetric complications, advanced paternal age or birth in winter are more or less in the same situation (Demjaha *et al.*, 2012).

Overall, the MHGP survey allowed to compare risk factors across a continuum ranging from bipolar disorder without psychotic features to psychotic disorders and observed the involvement of shared and specific environmental risk factors in these disorders with or without psychotic symptoms.

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