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Depression with and without a history of psychotic symptoms in the general population: sociodemographic and clinical characteristics

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ABSTRACT

Background: The aim of this study was to find the sociodemographic and clinical characteristics of major depressive episode (MDE) with (MDE-HPS+) and without a history of psychotic symptoms (MDE-HPS) in the general population.

Methods: The Mental Health in the General Population survey interviewed 38,694 individuals in France by using the MINI. The prevalence and sociodemographic and clinical correlates of MDE-HPS+ were assessed.

Results: Of the sample, 11.2% were diagnosed with current MDE and among them, 39.3% presented a history of at least one psychotic symptom (hallucination or delusion). Patients with MDE-HPS+ were younger with more severe social impairment than those with MDE-HPS-. We also found a higher proportion of three generations of migrants in the MDE-HPS+ group. Comorbid psychiatric disorders such as a history of a manic episode, alcohol use disorder, social anxiety, generalized anxiety disorder, and a personal history of a suicide attempt were more frequent in patients with MDE-HPS+ than in those with MDE-HPS-. Finally, we found a specific gradient of severity for psychiatric comorbid disorders depending on the number of psychotic symptoms lifetime in MDE.

Limitations: The study also has an observational cross-sectional design that does not permit causal inferences, and it is difficult to eliminate recall bias and reporting errors.

Conclusion: In the general population, patients with MDE-HPS+, when compared to MDE-HPS-, presented with a more severe clinical profile, with increased rates of psychiatric comorbidities, particularly a history of bipolar disorder and a history of a suicide attempt.

Keywords: major depressive episode; psychotic symptoms; continuum; suicide; bipolar disorder

INTRODUCTION

Major depressive episode (MDE) is one of the most common mental disorders worldwide, with a lifetime prevalence between 8% and 12% (Kessler and Bromet, 2013). It represents the heaviest burden of disability among mental and behavioural disorders (Hasin et al., 2018). MDE is characterized by several disabling symptoms affecting feelings, energy, cognition and daily activities, such as anhedonia, sadness, fatigue, loss of appetite, insomnia or hypersomnia (Malhi and Mann, 2018). Patients with MDE vary considerably in their clinical presentation, and several subtypes have been proposed based on specific symptom combinations (e.g., melancholic or psychotic depression), characteristics of onset (seasonal affective disorder, postpartum, early versus late onset), disease course (single, recurrent, chronic), or severity (Rush, 2007).

Major depression with psychotic features (hereafter psychotic depression, PD) is a severe subtype that corresponds to MDE associated with psychotic symptoms, including hallucinations and/or delusions (usually nihilistic delusions, such as overly self-critical or guilty beliefs). PD is usually considered as a debilitating mental disorder that requires intensive treatment and close monitoring (Dold et al., 2019). Indeed, PD displays severe clinical features, such as an increased risk of mortality, a higher risk to attempt suicide (Gournellis et al., 2018), or an increased care consumption (Nietola et al., 2018) in comparison with patients with non-psychotic MDE (No-PD).

Interestingly, in the general population, psychotic symptoms can be considered as a transdiagnostic phenomenon associated with greater severity and poorer functioning in multiple psychiatric disorders (van Os and Reininghaus, 2016). **Different theories of continuum exist : (i) the expression of psychosis is continuous across psychotic and non-psychotic disorders, (ii) isolated psychotic symptoms and schizotypal traits are attenuated versions of psychotic disorders, and (iii) the presence of isolated psychotic symptoms is predictive of further psychotic disorders** (Kaymaz et al., 2012). However, even if PD has been widely studied, data are very sparse about MDE with a history of psychotic symptoms (HPS).

In the present study, we aimed to explore the sociodemographic and clinical correlates of MDE patients with a history of psychotic symptoms (MDE-HPS+) compared to MDE patients without a history of psychotic symptoms (MDE-HPS-) in a large sample from the French general population. We also investigated the association between a history of psychotic symptoms and several clinical correlates and psychiatric comorbidities, such as a history of a manic episode, alcohol use disorders, anxiety disorders and a history of a suicide attempt in patients with MDE.

METHODS

The Mental Health in the General Population (MHGP) survey

The MHGP survey was conducted in France between 1999 and 2003. Overall, 38,694 subjects were included across 47 sites using a quota sampling method based on age, gender, educational level, and occupational category (Lunsford and Lunsford, 1995). Subjects were included in the study if they met the following criteria: 1) provided informed consent to participate in the survey, 2) were a French speaker, 3) were at least 18 years of age and 4) were neither institutionalized nor homeless. All interviewers (nurses and psychologists) were trained to administer the *Mini International Neuropsychiatric Interview* (MINI) using video recordings of interviews and role-plays over a 3-day session provided by *World Health Organization Collaborating Centre* (WHO-CC) experts. The MHGP study protocol was submitted to and approved by the "Comité consultatif sur le traitement de l'information en matière de recherche" (CCTIRS; #98.126).

Data collection

Sociodemographic characteristics (gender, income, education, marital status, and migrant status (first, second or third generation)) were collected. All participants were screened for psychiatric disorders using the MINI (ICD-10, French version, 5.0.0 (Sheehan et al., 1997)). The psychiatric disorders considered in the present study were current MDE (F32), alcohol use disorder (AUD) (i.e., dependence (F10.1) and abuse (F10.2)), a history of a manic episode (F30), panic disorder (F41.0 and F40.01), social anxiety disorder (SAD, F40.1), generalized anxiety disorder (GAD, F41.1), and post-traumatic stress disorder (PTSD, F43.1). Previous suicide attempts were also assessed.

Psychotic symptoms were screened with the "psychotic disorders" section of the MINI. The first five items assess the lifetime occurrence of delusional symptoms, i.e., delusions of persecution, thought broadcasting, delusions of control, delusions of reference, and other delusional ideas. The last two items assess the lifetime occurrence of visual and auditory hallucinations.

Additional details regarding the MHGP survey, including details about the screening of psychiatric disorders and psychotic symptoms, are available elsewhere (Amad et al., 2013; Pignon et al., 2018a).

Statistical analyses

Only subjects with MDE diagnosed with the MINI were considered. They were divided according to the **lifetime** history of at least one psychotic symptom (i.e., MDE-HPS+ or MDE-HPS-).

First, we aimed to assess the sociodemographic correlates of psychotic symptoms in subjects with MDE. We performed logistic regression analyses with all the sociodemographic variables: age, gender, income, education, marital status, and migrant status. Second, we aimed to assess the clinical correlates of psychotic symptoms. To this end, we performed logistic regression analyses with all the clinical variables: a history of a manic episode, AUD, panic disorder, SAD, GAD, PTSD, and a history of a suicide attempt. Sociodemographic variables were added as adjustment factors. Third, **we performed polytomous to assess the clinical correlates of different levels of psychotic symptoms: no psychotic symptoms, low level (1 or 2 psychotic symptom(s) endorsed), medium level (3 or 4 psychotic symptoms), and high level (between 5 and 7 psychotic symptoms), with “no-psychotic symptoms” as reference category.**

Because we aimed to exclusively assess psychotic symptoms in subjects with MDE, subjects with characterized psychotic disorders were excluded from the analyses.

All statistical analyses were performed using R software (<http://www.R-project.org/>).

RESULTS

Description of the sample

A total of 4,229 subjects (11.2% of the whole sample) were diagnosed with current MDE. Among them, 324 subjects with a co-occurring diagnosis of psychotic disorders were excluded, and 4015 subjects were thus finally included in the analyses. A total of 1,578 subjects (39.3%) displayed at least one lifetime psychotic symptom (MDE-HPS+ group), yielding a prevalence of 4% of subjects with MDE-HPS+ in the whole sample and including 1,081 (26.9%), 415 (10.3%) and 74 (1.8%) with low, medium and high levels of psychotic symptoms, respectively (missing data for 8 subjects). **Interestingly, bipolar depression (i.e. MDE with a history of a manic episode) was diagnosed in 148 subjects (3.7%). Among these 148 subjects, 101 (68.2%) were diagnosed MDE-HPS+. This rate was higher than in subjects with MDE without a history of a manic episode (N = 1477, 38.1 %, OR = 3.48 95 % CI [2.46-4.98], p < 0.001).**

The sociodemographic and clinical characteristics of the sample are available in **Supplementary Table 1.**

Sociodemographic characteristics

The results of the logistic regression analyses with the sociodemographic variables are presented in **Supplementary Table 2.** Subjects with MDE-HPS+ were younger (18-29 years OR= 2.42, 95% CI [1.85-3.17], p<0.001; 30-44 years: OR=1.90 [1.49-2.42], p<0.001; 45-59 years: OR=1.65 [1.30-2.10], p<0.001) and less educated (OR=1.34 [1.07-1.69], p= 0.011) than subjects with MDE-HPS-. Subjects with MDE-HPS+ also presented more often the "never married" (1.35 [1.13-1.61], p<0.001) and "separated" (OR=1.26 [1.01-1.57], p=0.038) status. Finally, the rates of migrants from the three generations were higher among subjects with MDE-HPS+ (first-generation migrant (OR=1.47 [1.13-

1.91], $p=0.004$); second-generation migrant (OR=1.25 [1.02-1.51], $p=0.027$); and third-generation migrant (OR=1.37 [1.10-1.69], $p=0.004$)).

Clinical characteristics

The prevalence of all psychiatric disorders except PTSD was higher among MDE-HPS+ subjects than among MDE-HPS- subjects (see **Table 1**). MDE-HPS+ was significantly associated with a history of a manic episode (OR=1.82 [1.21-2.75], $p=0.004$), alcohol use disorder (OR=1.36 [1.02-1.80], $p=0.034$), panic disorder (OR=2.08 [1.68-2.57], $p<0.001$), social anxiety disorder (OR=1.65 [1.28-2.11], $p<0.001$), generalized anxiety disorder (OR=1.48 [1.23-1.77], $p<0.001$), and a personal history of a suicide attempt (OR=1.61 [1.33-1.95], $p<0.001$).

Severity of psychotic symptoms

Co-occurring psychiatric disorders were more frequent in the MDE group following a gradient according to the level of psychotic symptoms (see **Table 2**).

DISCUSSION

In this study, we investigated the sociodemographic and clinical characteristics of MDE with a history of psychotic symptoms in a sample of 38,694 subjects from the French general population. The prevalence of MDE in our sample (11.2%) is consistent with the prevalence recently highlighted by a systematic review of the literature about the prevalence of MDE in France from 2000 to 2018 (about 10%) (Fond et al., 2019). We found that subjects with MDE-HPS+ (n=1,578) were younger, less educated and more often single than subjects with MDE-HPS-. The proportion of migrants among MDE-HPS+ subjects was also higher when compared to that among MDE-HPS-. In comparison to individuals with MDE-HPS-, those with MDE-HPS+ displayed a higher rate of psychiatric comorbidities, in particular, a history of a manic episode, alcohol use disorder, panic disorder, social anxiety disorder, generalized anxiety disorder and a history of a suicide attempt. Interestingly, we also found a gradient of severity for these psychiatric comorbidities depending on the number of psychotic symptoms.

A significant association between a personal history of a manic episode and the presence of a history of psychotic symptoms was found, with a gradient of severity of 5.4% in the low level, 7.7% in the medium level and 14.9% in the high level. This result confirmed the association between MDE-HPS+ and BD, as we found that MDE-HPS+ was significantly associated with a history of a manic episode. Interestingly, these results are consistent with several studies reporting that PD is associated with subsequent BD (Ostergaard et al., 2013).

The gender ratio was similar between MDE-HPS+ and MDE-HPS-. MDE-HPS+ patients also had more severe social impairment (lower education level, living more often alone (i.e., more “never married” or more “separated”)) than MDE-HPS- subjects. These results are consistent with previous findings (Gaudiano et al., 2016).

The presence of lifetime psychotic symptoms was also associated with a personal history of a suicide attempt. This agrees with a recent systematic review suggesting that the presence of

psychotic symptoms was associated with suicidal ideation, suicide attempts and completed suicides in the acute phase of MDE in comparison to patients without psychotic symptoms (Zalpur and Rothschild, 2016). Moreover, our results confirm that several risk factors for suicidal acts, such as psychotic symptoms or BD, may differ according to the mood disorder considered (Baldessarini et al., 2019). Interestingly, several disorders, such as anxiety disorders and alcohol use disorders, were also more frequently associated with MDE-HPS+ than MDE-HPS-. Several studies showed that when compared with patients with undifferentiated MDE, MDE-HPS+ patients present higher rates of current nicotine dependence, drug abuse/dependence (Leventhal et al., 2008), alcohol use disorder and anxiety disorder (Nietola et al., 2018).

Finally, we highlighted a gradient of severity depending on the number of lifetime psychotic symptoms associated with the MDE. In particular, a personal history of a manic episode, a personal history of a suicide attempt, alcohol use disorder, and anxiety disorders were all strongly associated with the number of psychotic symptoms. This result is particularly interesting considering the continuum model of psychosis, which suggests that psychotic symptoms are associated with broad psychiatric disorders (McGrath et al., 2016; Pignon et al., 2018b). Thus, a history of psychotic symptoms appears to be associated with worse outcomes in both subjects with and without psychiatric disorders, following a gradient of severity increasing with the number of psychotic symptoms.

Some limitations of our study must be considered. Regarding the probabilistic sampling method using a quota within a region, we cannot assume that our sample was representative of the general population. **This method develops a sample of subjects with the same characteristics as the general population on predefined characteristics, such as age, sex, educational level, occupational category, and professional status (according to census figures from 1999 provided by the French National Institute for Statistics and Economic Studies)** (Caria et al., 2010). Other limitations of this study, such as the French-speaking inclusion criterion and the absence of data concerning the subjects that refused to participate, have already been discussed elsewhere (Pignon et al., 2018a), as

was the fact that homeless and/or hospitalized people, those under 18 years of age, and non-French-speaking people were excluded from the sample (Pignon et al., 2018a). It should also be noted that no participation rate was assessed in this study and that no specific reliability study of the MINI was undertaken. Moreover, the collected data were relatively old (between 1999-2003), but it is very unlikely that MDE-HPS+ patients are different at present. The study also has an observational cross-sectional design that does not permit causal inferences, and it is difficult to eliminate recall bias and reporting errors. Finally, other factors could be taken into account, such as treatment and personality disorders that may be associated with psychotic symptoms, but these data were not available in this study.

Future studies should include well characterised and larger samples of patients assessed by specific scale such as the Psychotic Depression Assessment Scale (PDAS) (Østergaard et al., 2014). These studies could compare specific clinical and biological features such as sociodemographic variables (e.g. age of onset), treatment response, biological abnormalities, sleep or circadian rhythms alteration between patients with MDE-HPS+ vs MDE-HPS- and in PD in comparison with patients with no PD. It would be essential to find if these characteristics allow to distinguish patients with bipolar and unipolar disorder.

In conclusion, in the general population, MDE-HPS+, when compared to MDE-HPS-, presented with a higher probability of more severe profile, with increased rates of psychiatric comorbidities, particularly a history of a manic episode and a history of a suicide attempt. Considering that, the history of psychotic symptoms should always be explored in patients with MDE, as well as the opportunity to prescribe a mood stabiliser, especially in treatment resistant depression. ~~These results support the continuum model of psychosis.~~ Psychotic symptoms could be present in the general population and in broad psychotic disorders with a gradient of severity depending on the number of psychotic features.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Conflict of interest: The authors have declared that there are no conflicts of interest in relation to the subject of this study.

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Ethical standards: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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MDE with a history of psychotic symptoms		
(N = 1,578)		
	OR [95 % CI]	<i>p</i> ²
History of manic episode	1.82 [1.21-2.75]	0.004
Alcohol use disorder	1.36 [1.02-1.80]	0.034
Panic disorder	2.08 [1.68-2.57]	< 0.001
Social anxiety disorder	1.65 [1.28-2.11]	< 0.001
Generalized anxiety disorder	1.48 [1.23-1.77]	< 0.001
Post-traumatic stress disorder	1.14 [0.66-1.96]	0.640
Personal history of suicide attempts	1.61 [1.33-1.95]	< 0.001

Table 1. Clinical correlates of lifetime psychotic symptoms among subjects with major depressive episode (MDE)¹

¹After the exclusion of characterized psychotic disorders validated by a clinician;

²Logistic binomial regression adjusted for age, gender, educational level, income level, marital status and migrant status (except for the index variable);

³Monthly income levels: low: <1,650 €/household; medium: 1,650-3,200 €/household; high: >3,200 €/household

	Low level of psychotic symptoms (1-2 psychotic symptom(s)) (N = 1081)			Medium level of psychotic symptoms (3-4 psychotic symptoms) (N = 415)			High level of psychotic symptoms (5-6-7 psychotic symptoms) (N = 74)		
	N (%)	OR [95 % IC]	p	N (%)	OR [95 % IC]	p	N (%)	OR [95 % IC]	p
Age-band									
18-29 years	364 (33.7)	1.95 [1.37-2.77]	< 0.001	168 (40.5)	2.28 [1.32-3.94]	0.003	26 (35.1)	2.21 [0.64-7.66]	0.210
30-44 years	323 (29.9)	1.49 [1.08-2.04]	0.014	121 (29.2)	1.61 [0.96-2.67]	0.069	28 (37.8)	2.12 [0.66-6.8]	0.208
45-59 years	201 (18.6)	1.43 [1.04-1.96]	0.025	82 (19.8)	1.74 [1.05-2.88]	0.032	13 (17.6)	2.32 [0.73-7.37]	0.154
60+ years (reference)	193 (17.9)	-	-	44 (10.6)	-	-	7 (9.5)	-	-
Gender									
Male (reference)	422 (39.9)	-	-	177 (42.7)	-	-	33 (44.6)	-	-
Female	659 (61)	0.84 [0.7-1.02]	0.074	238 (57.3)	0.91 [0.69-1.2]	0.506	41(55.4)	1.06 [0.58-1.93]	0.842
Education level									
No education-elementary level	282 (26.1)	1.24 [0.92-1.68]	0.153	85 (20.5)	0.95 [0.61-1.48]	0.822	18 (24.3)	1.3 [0.52-3.25]	0.579
College level	591(54.7)	1.2 [0.95-1.52]	0.126	244 (58.8)	1.14[0.82-1.59]	0.432	39 (52.7)	1.12 [0.54-2.3]	0.764
University level (reference)	208(19.2)	-	-	86 (20.7)	-	-	17 (23)	-	-
Income level¹									
Low	569 (52.6)	0.99 [0.75-1.31]	0.937	218 (52.5)	1.15 [0.76-1.75]	0.504	42 (56.8)	0.75 [0.34-1.67]	0.483
Medium	339 (31.4)	0.9 [0.68-1.18]	0.442	125 (30.1)	0.99 [0.65-1.5]	0.959	21 (28.4)	0.61[0.27-1.39]	0.236
High (reference)	136 (12.6)	-	-	51 (12.3)	-	-	10 (13.5)	-	-
Marital status									
Married (reference)	421 (38.9)	-	-	149 (35.9)	-	-	24 (32.4)	-	-
Never married	412 (38.1)	1.32 [1.04-1.67]	0.025	187 (45.1)	1.45 [1.03-2.03]	0.032	36 (48.6)	1.59 [0.79-3.23]	0.196
Separated	137 (12.7)	1.18 [0.88-1.58]	0.259	56 (13.5)	1.26 [0.83-1.9]	0.277	10 (13.5)	1.11 [0.46-2.72]	0.816
Widowed	107(9.9)	1.32 [0.94-1.86]	0.114	22(5.3)	0.93 [0.51-1.7]	0.809	4 (5.4)	0.54 [0.11-2.76]	0.463
Migrant status									
Native ²	708 (65.5)	-	-	243 (58.6)	-	-	40 (54.1)	-	-
1GM ³	77 (7.1)	1.3 [0.91-1.86]	0.153	41 (9.9)	2.12 [1.34-3.37]	0.001	7 (9.5)	2.34 [0.91-5.98]	0.077
2GM ⁴	155 (14.3)	1.08 [0.83-1.39]	0.579	76 (18.3)	1.5 [1.06-2.13]	0.022	21 (28.4)	3 [1.59-5.7]	0.001
3GM ⁵	141 (13)	1.72 [1.31-2.25]	< 0.001	55(13.3)	1.55 [1.04-2.3]	0.030	6 (8.1)	0.97 [0.33-2.85]	0.954
Psychiatric disorders									
History of manic episode	58 (5.4)	1.73 [1.1-2.73]	0.017	32 (7.7)	1.75 [1.01-3.06]	0.048	11 (14.9)	3.15 [1.36-7.33]	0.008
Alcohol use disorders	104 (9.6)	1.09 [0.79-1.51]	0.591	71 (17.1)	1.77 [1.19-2.62]	0.005	20 (27)	2.9 [1.42-5.95]	0.004
Panic disorder	258 (24)	1.97 [1.55-2.49]	< 0.001	121 (29.2)	2.00 [1.43-2.78]	< 0.001	30 (40.5)	6.46 [2.97-14.05]	< 0.001
Social anxiety disorder	156 (14.4)	1.6 [1.21-2.1]	0.001	72 (17.3)	1.84 [1.27-2.66]	0.001	14 (18.9)	1.7 [0.77-3.77]	0.188
Generalized anxiety disorder	323 (29.9)	1.44 [1.18-1.76]	< 0.001	133 (32)	1.39 [1.03-1.89]	0.033	26 (35.1)	4.24 [1.97-9.11]	< 0.001
Post-traumatic stress disorder	20 (1.9)	0.88 [0.46-1.69]	0.696	19 (4.6)	1.59 [0.78-3.22]	0.200	4 (5.4)	2.18 [0.68-7.03]	0.191
History of suicide attempts	197 (18.2)	1.38 [1.11-1.71]	0.004	119 (28.7)	2.38 [1.79-3.15]	< 0.001	20 (27)	1.49 [0.81-2.73]	0.202

Table 2. Sociodemographic and clinical characteristics and correlates of the subjects with major depressive episode and a history of psychotic symptoms according to the number of psychotic symptoms, in comparison to subjects with major depressive episode and without a history of psychotic symptoms

¹Monthly income levels: low<1,650 €/household; medium: 1,650-3,200 €/household; high: >3,200 €/household;

²Subject who was born and whose parents and grandparents were born in metropolitan France;

³1GM: First-generation migrant;

⁴2GM: Second-generation migrant;

⁵3GM: Third-generation migrant.