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ORIGINAL ARTICLE

Impact of a family history of mental disorders on the characteristics of patients with early psychosis

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Abstract

Aim: Children of parents with psychiatric illness have a higher risk of developing psychiatric disorders. This is particularly the case for psychoses and the evolution of these disorders could likely differ. The aim of this study was to study the impact of a first-degree and second-degree family history of psychiatric disorders (FHPD) on the characteristics of patients with early psychosis in a specialized programme.

Method: This research is a prospective study based on 408 patients aged 18–35 years enrolled in the Treatment and Early Intervention in Psychosis Program (TIPP) with a three-years follow-up. Various characteristics were compared between patients with first-degree-FHPD and those without, then between patients with 2nd degree-FHPD and those without. The influence of the number of parents with first or second degree FHPD on clinical characteristics was also studied.

Results: Our results showed an influence of FHPD on the characteristics of patients presenting a first episode of psychosis. Over the 3 years of follow-up, patients with at least one second-degree relative showed more negative and depressive symptoms and poorer general functioning than patient who did not. The number of parents with first or second degree FHPD was also negatively associated with several clinical variables.

Conclusion: The results of this study confirm the existence of a distinct premorbid profile and a different evolution in patients with FHPD, which is not limited to first-degree relatives. This suggests the importance of specific needs that should be addressed during treatment.

KEYWORDS
family history, premorbid features, psychosis, remission, treatment

1 | INTRODUCTION

Affecting between 0.5% and 2% of the population (Gourier-Frery et al., 2014), psychoses are a heterogeneous group of relatively frequent illnesses (Esterberg & Compton, 2012) with a transgenerational and multifactorial transmission (Morley et al., 2008). The literature shows that having a family member with a psychotic disorder increases the risk of developing psychosis, with a higher likelihood if they are first degree relatives and a cumulative effect depending on the number of relatives (father, mother or siblings) (Naber, 2009). Some data also suggest that family history of psychiatric disorders (FHPD) could impact the course of psychosis in the off-springs (Dean

et al., 2010; Hameed & Lewis, 2016; Kessler et al., 2010; McLaughlin et al., 2012; Morley et al., 2008; van Santvoort et al., 2015; Weissman et al., 2016).

The literature does not offer an unequivocal picture of the characteristics of patients with FHPD. For instance, several studies suggest that FHPD correlates with earlier age of onset of psychotic symptoms (Esterberg et al., 2010; Esterberg & Compton, 2012; Ritsner et al., 2007; Suvisaari et al., 1998) while others do not (Compton et al., 2017; Yu-Hai Chen et al., 2005). Similarly, some studies suggest a link between FHPD and duration of the prodromal phase (PD) and untreated psychosis (DUP), but either with shorter or longer duration while some do not show any link (Esterberg & Compton, 2012; Morley et al., 2008; Norman et al., 2007; Yu-Hai Chen et al., 2005). With regard to premorbid characteristics, that is, characteristics before the onset of the disease, the literature suggest no evident relationship between FHPD and patient's gender (Esterberg & Compton, 2012; Ritsner et al., 2007; Yu-Hai Chen et al., 2005), or educational level (Yu-Hai Chen et al., 2005).

Regarding the characteristics of patients at the time of entry into treatment and throughout treatment, the results of the literature are again not consistent. Substance abuse for instance was either increased or decreased depending on the study (Morley et al., 2008; Sarrazin et al., 2015; Sevy et al., 2001). Similarly, there were discrepancies about the relationship between FHPD and disease severity as measured by various functional scores, with some studies showing no difference (Morley et al., 2008) and others describing a poorer functioning (Jarbin et al., 2003). Interestingly, only one study distinguished between the impact of first-degree FHPD (father, mother or siblings) and second-degree FHPD (grandfather/mother, uncle, aunt): no difference between the two groups were highlighted with regard to socio-demographic characteristics, symptoms and emotional distress at baseline, as well as after 16 months of follow-up (Ritsner et al., 2007).

With regard to psychotic and depressive symptoms, results suggested that although there was no difference at the beginning of treatment, there was less improvement in patients with FHPD (Esterberg & Compton, 2012; Käkelä et al., 2018; Ritsner et al., 2007). The literature also showed less compliance with medication and more frequent childhood trauma in children with a family history of psychotic disorders, factors that are, in turn, linked to poorer functioning (Alameda et al., 2015; Kelleher et al., 2013). If we take an interest on outcomes, FHPD was shown to negatively affect outcome in some studies (Conus et al., 2006; Jarbin et al., 2003; Käkelä et al., 2018; Suvisaari et al., 1998) but results are not consistent: other studies showed for instance no evident association with symptomatic remission (Conus et al., 2006), nor with functional remission (Käkelä et al., 2018; Morley et al., 2008).

In summary, there are many discrepancies in the literature, which may be due to the many methodological differences between studies (for instance considering family history of psychosis or family history of psychiatric illness). However, overall, results still seem to suggests a less favourable profile in patients with FHPD.

Considering these elements, we wanted to investigate the issue of the potential impact of a FHPD on the characteristics of patients with early psychosis in the cohort of the specialized Treatment and Early Intervention in Psychosis Program (TIPP). We focused on FHPD rather than family history of psychosis because we hypothesized that, above and over genetic vulnerabilities, the familial context could be impacted by other psychiatric disorders and not only by psychosis. We set ourselves several goals: The first objective was to compare premorbid, clinical and outcome characteristics between patients who had at least one first-degree parent with a psychiatric disorder and patients who did not. The second objective was to compare patients who had at least one second-degree parent with a psychiatric disorder (but no first-degree parent with psychiatric disorder) and patients who did not. Finally, our third objective was to study the influence of the number of relatives with a mental disorder on these characteristics.

2 | MATERIALS AND METHODS

2.1 | Participants

The participants in our study were recruited from the TIPP (Treatment and early Interventions in Psychosis Program), which aims to provide integrated care for patients experiencing a first episode of psychosis (Conus et al., 2010). The criteria for inclusion in the study were the same as those for entry into the programme, that is, (i) patients aged 18–35 years with a first episode of psychosis, (ii) living in the Lausanne area and surroundings and (iii) meeting the Comprehensive Assessment of the At-Risk Mental States (CAARMS) criteria for threshold psychosis (Alameda et al., 2015; Yung et al., 2005). Patients were referred to other programmes and therefore excluded from this study if they had been taking antipsychotics for more than 6 months in total before entering the programme, if they had psychosis related to intoxication or organic brain disease, or if they had an IQ below 70 (Alameda et al., 2015).

Patients are regularly followed up for 3 years (at entry, after 2 months, 6 months and then every 6 months) by case managers and various information is collected on their demographic characteristics, history, symptoms, functioning, treatment and course (Alameda et al., 2015; General Psychiatry Service, Department of Psychiatry, & Lausanne University Hospital, 2021). The diagnosis is made by a psychiatrist and re-evaluated at the end of the follow-up on the basis of DSM IV criteria (Alameda et al., 2015; American Psychiatric Association, 1994).

The Cantonal Commission for Ethics in Human Research (CER-VD) granted access to the TIPP clinical data for research purposes (request #2020-00272). The clinical data generated by the follow-up of all patients were used in the study if the patients did not explicitly object to the use of their data for research purposes. Only four patients refused the use of their clinical data for research. This work is a prospective study based on the 408 patients who were enrolled in the programme and had been treated for 36 months at the start of this study.

TABLE 1 Sociodemographic, clinical data according to presence of first degree relative with psychiatric disorder.

	No family history	First degree family history only		95% CI of OR		
	N = 220	*N* = 106	Odds ratio (OR)	LCI	UCI	*p*-Value
Gender, female, % (*N*)	32.7 (72)	36.8 (39)	1.010	0.609	1.673	.970
Age in year, M (SD)	24.64 (4.86)	24.81 (4.65)	1.000	0.951	1.051	.996
Duration of untreated psychosis, Mdn (IQR)[a]	91.50 (354.75)	86.00 (459.25)	1.020	0.754	1.381	.897
Age of onset in year, M (SD)	23.44 (4.92)	23.33 (5.01)	0.990	0.943	1.039	.674
Socio-economical level, % (*N*)			1.251	.907	1.725	.172
Low	28.6 (63)	17.0 (18)				
Intermediate	36.4 (80)	52.8 (56)				
High	35.0 (77)	30.2 (32)				
Education in year, M (SD)	10.13 (2.58)	10.04 (2.85)	1.000	0.909	1.100	.997
Marital status, % (N)						
Single	85.6 (184)	77.1 (81)	Ref.cat.	–	–	–
Married	10.2 (22)	11.4 (12)	1.000	0.456	2.194	.999
Divorced	1.4 (3)	3.8 (4)	2.726	0.574	12.940	.207
Cohabitation	2.8 (6)	7.6 (8)	2.469	0.783	7.788	.123
Professional activity, % (*N*)						
Unemployed	49.8 (107)	43.3 (45)	Ref.cat.	–	–	–
Full or part time job	8.4 (18)	17.3 (18)	2.733	1.271	5.877	.010
Student/Traineeship	20.5 (44)	14.4 (15)	1.041	0.512	2.119	.911
Disability annuity	2.8 (6)	1.0 (1)	0.433	0.049	3.809	.450
On Sickness leave	18.6 (40)	24.0 (25)	1.705	0.906	3.207	.098
Lifestyle, % (*N*)						
Independent household	20.3 (43)	28.2 (29)	Ref.cat.	–	–	–
With friends	26.4 (56)	18.4 (19)	0.519	0.253	1.066	.074
Family	44.3 (94)	43.7 (45)	0.797	0.434	1.467	.467
Pension/care home	3.8 (8)	3.9 (4)	0.713	0.191	2.663	.615
Unsettled (hotel, shelter homeless)	5.2 (11)	5.8 (6)	0.645	0.208	2.002	.448
Premorbid Adj. (PAS) M (SD)						
Childhood	0.29 (0.19)	0.33 (0.18)	1.700	0.418	6.914	.459
Early adolescence	0.30 (0.18)	0.35 (0.17)	3.035	0.719	12.810	.131
Social	0.27 (0.22)	0.30 (0.21)	1.319	0.388	4.489	.657
Academic	0.34 (0.21)	0.39 (0.20)	2.645	0.744	9.404	.133
Total	0.30 (0.18)	0.33 (0.17)	2.065	0.428	9.962	.366
Past suicide attempt, % (*N*)	12.6 (26)	12.7 (13)	0.885	0.425	1.841	.744
History of trauma[b], % (*N*)	26.0 (56)	45.7 (48)	2.391	1.465	3.903	<.001
Migration in adversity, % (*N*)	34.1 (75)	23.6 (25)	0.444	0.252	0.783	.005
Forensic history, % (*N*)	16.8 (31)	16.1 (15)	0.834	0.414	1.677	.610
Offences during program, % (*N*)	13.2 (19)	8.5 (5)	0.549	0.191	1.575	.265
Psychiatric history, % (*N*)	54.0 (115)	65.0 (67)	1.491	0.904	2.459	.118
Lifetime substance abuse (DSM), % (N)						
Alcohol	16.4 (35)	27.5 (28)	1.892	1.057	3.387	.032
Cannabis	32.1 (68)	36.5 (38)	1.283	0.774	2.129	.334
Other substances	9.8 (21)	12.4 (13)	1.156	0.544	2.458	.706
Lifetime substance dependance (DSM), % (*N*)						
Alcohol	3.3 (7)	8.8 (9)	2.368	0.834	6.722	.105

(Continues)

TABLE 1 (Continued)

	No family history	First degree family history only		95% CI of OR		
	$N = 220$	$N = 106$	Odds ratio (OR)	LCI	UCI	*p*-Value
Cannabis	25.6 (54)	30.8 (32)	1.326	0.779	2.254	.298
Other substances	4.7 (10)	5.7 (6)	1.110	0.382	3.222	.848
Substance use remitted, % (*N*)[c]						
No SUD	63.9 (122)	55.3 (52)	Ref.cat.	–	–	–
Decreased	17.8 (34)	18.1 (17)	0.607	0.326	1.129	.115
Persistent	18.3 (35)	26.6 (25)	0.767	0.347	1.697	.513
Insight at presentation, % (*N*)			1.021	0.730	1.429	.903
Absent	34.0 (72)	31.4 (32)				
Partial	44.3 (94)	50.0 (51)				
Complete	21.7 (46)	18.6 (19)				
GAF, M (SD)						
Baseline	42.95 (17.33)	40.36 (16.49)	0.991	0.977	1.006	.245
Worst during psychosis	29.09 (11.53)	26.48 (10.98)	0.980	0.959	1.002	.070
SOFAS, M (SD)						
Baseline	43.72 (16.19)	41.49 (15.93)	0.993	0.978	1.008	.364
Worst during psychosis	30.29 (11.41)	28.43 (11.46)	0.987	0.966	1.009	.254
CGI, M (SD)						
Baseline	4.36 (1.47)	4.78 (1.36)	1.225	1.011	1.485	.039
Higher during psychosis	5.72 (0.77)	5.78 (0.83)	0.987	0.966	1.009	.254
Diagnostic, % (*N*)						
Schizophrenia	60.0 (132)	52.8 (56)	Ref.cat.	–	–	–
Schizophreniform/brief	14.1 (31)	14.2 (15)	1.277	.629	2.596	.499
Schizo-affective	6.8 (15)	9.4 (10)	1.367	.554	3.373	.497
Major depression[d]	4.5 (10)	4.7 (5)	1.175	.375	3.678	.782
Bipolar disorder	5.0 (11)	5.7 (6)	1.490	.515	4.313	.462
Other	9.5 (21)	13.2 (14)	1.695	.774	3.709	.187

Abbreviations: IQR, interquartile range; Mdn, median; Ref. cat., reference category.
[a]Raw data are presented, however the test statistics were based on log10 (+constant) transformed data because of extreme positive skewness.
[b]Physical, emotional or sexual abuse.
[c]Comparison between baseline and maximum value between 18 and 36 months.
[d]With psychotic features. All analyses were adjusted for trauma.

2.2 | Family history of mental disorder (FHPD)

The presence of a FHPD was collected at entry into the programme and could be updated by the case managers following various interactions with patients and their families. The following diagnostics were considered: schizophrenia, schizophreniform disorder, bipolar disorder, depression, OCD, anxiety disorder, substance abuse, alcohol abuse, personality disorder, and other relevant mental disorders. We defined family psychiatric history as (i) no clinically significant FHPD; (ii) First-degree FHPD only (that is, at least one person between father, mother and siblings with a mental disorder); (iii) Second-degree FHPD only (that is, at least one person between grandparents, uncle and aunt with a mental disorder). In this paper, patients who had no clinically significant FHPD were compared firstly to patients with first degree FHPD and secondly to patients with second degree FHPD on various pre-morbid and outcome variables.

2.3 | Other clinical and socio-demographic characteristics

Socio-demographic data such as gender, socio-economic level, occupation, lifestyle, but also age of onset of psychosis, and DUP were recorded. Exposure to traumatic events in the past was also collected, such as adoption, parental separation, abuse, death of a relative, migration in adversity, neglect and abandonment. The patient's

TABLE 2 Outcome data according to presence of first degree relative with psychiatric disorder.

	No family history	First degree family history only		95% CI of OR		
	$N = 220$	$N = 106$	Odds ratio (OR)	LCI	UCI	*p*-Value
Program commitment, % (*N*)Lost from sight	16.0 (24)	10.0 (8)	0.665	0.278	1.587	.358
Symptomatic response at the last assessment of the last year of the program (Andreassen), % (*N*)	53.3 (49)	51.7 (31)	1.070	0.540	2.122	.846
Functional recovery (PAS) at the last assessment of the last year of the program, % (*N*)	50.7 (74)	45.7 (37)	0.784	0.448	1.373	.396
Functional recovery (GAF ≥60), % (N)	60.3 (85)	46.1 (35)	0.649	0.363	1.162	.146
Functional recovery—independent work, % (*N*)	36.5 (54)	23.5 (19)	0.595	0.318	1.115	.105
Functional recovery—independent living, % (*N*)	59.9 (88)	68.3 (56)	1.338	0.745	2.401	.330
Combined functional recovery (indep. work & living), % (*N*)	27.9 (41)	19.8 (16)	0.714	0.365	1.398	.326

Note: All analyses were adjusted for trauma.
Abbreviation: Ref. cat., reference category.

psychiatric history was also compared, as well as substance abuse and dependence (alcohol, cannabis and others) according to DSM-IV criteria (American Psychiatric Association, 1994).

The lower level of functioning and higher level of symptoms achieved during psychosis were estimated using the Clinical Global Impression (CGI), the Social and Occupational Functioning Assessment Scale (SOFAS) and the Global Assessment of Functioning (GAF) scales. These dimensions were also assessed at the beginning of the programme and throughout the follow-up. During the latter, psychotic symptoms were assessed by the Positive and Negative Symptom Scale (PANSS) and depressive symptoms by the Montgomery-Åsberg Depression Rating Scale (MADRS). Medication compliance was also assessed by the case managers.

The outcome at the end of the programme was measured through the following variables: dropouts, symptomatic and functional remission (return to the initial level according to the Premorbid Assessment Scale (PAS) and a GAF score > 60), as well as recovery of occupation (return to work or studies) and lifestyle (independent housing).

2.4 | Statistical analysis

We first verified whether the groups differed for important sociodemographic and clinical characteristics (gender, age, DUP, socioeconomic level, diagnostic & trauma) in order to control for potential variation in following analyses. Since we found a higher prevalence of trauma exposure in patients with 1st degree FHPD (OR = 2.391, $p = .001$) and a higher socioeconomic level in those with 2nd degree FHPD (OR = 1.604, $p = .040$) we controlled for these factors in all subsequent analyses. For that purpose and to make all comparisons within the same metric, we estimated a series of logistic regressions with group membership as the dependent variable and the different test variables, as well as trauma, respectively socio-economic level, as independent variables. To compare the level of functioning between the groups at follow-up, we estimated repeated measures mixed models (MMRM). Finally, to investigate the relationship between the number of parents with first or second degree FHPD and the different variables, non-parametric correlations or Mann–Whitney *U* tests were used. Patients with both first- and second-degree parents with psychiatric disorder were excluded from the group comparisons but were considered when studying the influence of the number of relatives with a mental disorder. All analyses were conducted with IBM SPSS version 27 software.

3 | RESULTS

A total of 408 patients were included. About half ($N = 220$, 54%) of the patients did not have relatives with psychiatric disorders. 106 patients (26.0%) had first degree FHPD only and 41 patients (10.0%) had second degree FHPD only. Finally, 41 patients (10.0%) had both first- and second-degree FHPD. All comparisons were made between patients without FHPD and the other subgroups.

Patients with a first-degree FHPD were more likely to have been exposed to trauma (OR = 2.391, $p < .001$) but less likely to have experienced migration in adversity (OR = 0.444, $p = .005$; Table 1). They were more likely to have a part- or a full-time job (OR = 1.271, $p = .010$). They were also more likely to suffer from alcohol abuse (OR = 1.892, $p = .032$) and showed a higher CGI score (OR = 1.225, $p = .039$) at the entry in the program.

No statistically significant differences were highlighted on three-years outcomes (Table 2).

Patients with a second-degree FHPD had higher socio-economical level (OR = 1.604, $p = .040$) and were more likely to have a psychiatric history (OR = 2.342, $p = .026$; Table 3). They were also more likely to suffer from alcohol dependence (OR = 4.405, $p = .017$).

Patients with a second-degree FHPD were also less likely to attain work-related functional recovery (OR = 0.270, $p = .011$) and

TABLE 3 Sociodemographic, clinical data according to presence of second degree relative with psychiatric disorder.

	No family history	Second degree family history only		95% CI of OR		
	$N = 220$	$N = 41$	Odds ratio (OR)	LCI	UCI	*p*-Value
Gender, female, % (*N*)	32.7 (72)	34.1 (14)	1.131	0.554	2.306	.736
Age in year, M (SD)	24.64 (4.86)	23.51 (4.27)	0.951	0.883	1.025	.190
Duration of untreated psychosis, Mdn (IQR)[a]	91.50 (354.75)	75.00 (540.50)	0.833	0.551	1.259	.386
Age of onset in year, M (SD)	23.44 (4.92)	22.56 (5.18)	0.965	0.899	1.035	.322
Socio-economical level, % (*N*)			1.604	1.022	2.518	.040
Low	28.6 (63)	12.2 (5)				
Intermediate	36.4 (80)	41.5 (17)				
High	35.0 (77)	46.3 (19)				
Education in year, M (SD)	10.13 (2.58)	9.97 (2.41)	0.922	0.792	1.074	.298
Marital status, % (*N*)						
Single	85.6 (184)	92.7 (38)	Ref. cat.	–	–	–
Married	10.2 (22)	0.0 (0)	0.000	0.000	–	.998
Divorced	1.4 (3)	2.4 (1)	1.940	0.193	19.510	.573
Cohabitation	2.8 (6)	4.9 (2)	1.408	0.269	7.367	.685
Professional activity, % (N)						
Unemployed	49.8 (107)	46.2 (18)	Ref. cat.	–	–	–
Full or part time job	8.4 (18)	12.8 (5)	1.384	0.447	4.281	.573
Student/Traineeship	20.5 (44)	15.4 (6)	0.665	0.242	1.830	.430
Disability annuity	2.8 (6)	2.6 (1)	0.790	0.088	7.118	.833
On Sickness leave	18.6 (40)	23.1 (9)	1.264	0.520	3.073	.605
Lifestyle, % (*N*)						
Independent household	20.3 (43)	14.6 (6)	Ref. cat.	–	–	–
With friends	26.4 (56)	19.5 (8)	0.969	0.310	3.032	.957
Family	44.3 (94)	51.2 (21)	1.609	0.601	4.306	.344
Pension/care home	3.8 (8)	7.3 (3)	2.984	0.600	14.838	.182
Unsettled (hotel, shelter homeless)	5.2 (11)	7.3 (3)	1.836	0.389	8.680	.443
Premorbid Adj. (PAS) M (SD)						
Childhood	0.29 (0.19)	0.31 (0.19)	1.961	0.280	13.729	.498
Early adolescence	0.30 (0.18)	0.32 (0.20)	2.167	0.265	17.713	.471
Social	0.27 (0.22)	0.30 (0.22)	1.760	0.335	9.249	.504
Academic	0.34 (0.21)	0.35 (0.20)	1.695	0.262	10.979	.580
Total	0.30 (0.18)	0.32 (0.19)	2.368	0.257	21.791	.447
Past suicide attempt, % (*N*)	12.6 (26)	22.5 (9)	1.825	0.772	4.315	.171
History of trauma[b], % (*N*)	26.0 (56)	29.3 (12)	1.350	0.633	2.878	.438
Migration in adversity, % (*N*)	34.1 (75)	22.0 (9)	0.647	0.287	1.462	.295
Forensic history, % (*N*)	16.8 (31)	7.9 (3)	0.483	0.138	1.691	.255
Offences during program, % (*N*)	13.2 (19)	5.6 (1)	0.473	0.058	3.852	.484
Psychiatric history, % (*N*)	54.0 (115)	73.2 (30)	2.342	1.109	4.946	.026
Lifetime substance abuse (DSM), % (*N*)						
Alcohol	16.4 (35)	23.1 (9)	1.464	0.634	3.380	.372
Cannabis	32.1 (68)	33.3 (13)	1.022	0.492	2.124	.954
Other substances	9.8 (21)	14.6 (6)	1.511	0.563	4.050	.412
Lifetime substance dependance (DSM), % (*N*)						
Alcohol	3.3 (7)	12.8 (5)	4.405	1.298	14.947	.017

TABLE 3 (Continued)

	No family history	Second degree family history only		95% CI of OR		
	N = 220	*N* = 41	Odds ratio (OR)	LCI	UCI	*p*-Value
Cannabis	25.6 (54)	23.1 (9)	0.836	0.371	1.885	.665
Other substances	4.7 (10)	9.8 (4)	2.071	0.608	7.059	.245
Substance use remitted, % (*N*)[c]						
No SUD	63.9 (122)	50.0 (18)	Ref. cat.	–	–	–
Decreased	17.8 (34)	16.7 (6)	0.460	0.200	1.062	.069
Persistent	18.3 (35)	33.3 (12)	0.512	0.170	1.545	.235
Insight at presentation, % (*N*)			1.049	0.662	1.663	.838
Absent	34.0 (72)	30.0 (12)				
Partial	44.3 (94)	47.5 (19)				
Complete	21.7 (46)	22.5 (9)				
GAF, M (SD)						
Baseline	42.95 (17.33)	38.75 (14.90)	0.985	0.964	1.005	.145
Worst during psychosis	29.09 (11.53)	28.81 (12.77)	1.000	0.970	1.032	.978
SOFAS, M (SD)						
Baseline	43.72 (16.19)	41.31 (15.69)	0.989	0.968	1.010	.308
Worst during psychosis	30.29 (11.41)	31.00 (12.43)	1.006	0.975	1.038	.717
CGI, M (SD)						
Baseline	4.36 (1.47)	4.88 (0.99)	1.343	0.996	1.811	.053
Higher during psychosis	5.72 (0.77)	5.73 (.80)	1.006	0.975	1.038	.717
Diagnostic, % (*N*)						
Schizophrenia	60.0 (132)	56.1 (23)	Ref. cat.	–	–	–
Schizophreniform/brief	14.1 (31)	7.3 (3)	0.545	0.153	1.943	.349
Schizo-affective	6.8 (15)	12.2 (5)	1.873	0.613	5.721	.271
Major depression[d]	4.5 (10)	0.0 (0)	0.000	0.000	–	.999
Bipolar disorder	5.0 (11)	7.3 (3)	1.405	0.358	5.521	.626
Other	9.5 (21)	17.1 (7)	2.194	0.818	5.886	.119

Abbreviations: IQR, interquartile range; Mdn, median; Ref. cat., reference category.
[a]Raw data are presented, however the test statistics were based on log10 (+constant) transformed data because of extreme positive skewness.
[b]Physical, emotional or sexual abuse.
[c]Comparison between baseline and maximum value between 18 and 36 months.
[d]With psychotic features. All analyses were adjusted for SES.

combined work and independent living recovery (OR = 0.321, $p = .045$) at the end of the programme (Table 4).

Results of the longitudinal analysis revealed no differences between patients who had a first-degree FHPD and patients who did not over the three-years of follow-up. Nevertheless, patients with second-degree FHPD scored on average 2.04 points higher on the PANSS negative scale over the 3 years than patients who did not ($F_{(1,151.202)} = 4.898$, $p = .028$; Figure 1). A similar pattern was highlighted for the depression score where patients with second-degree FHPD scored on average 3.62 points higher on the MADRS scale over three-years ($F_{(1,178.349)} = 7.539$, $p = .007$). Examination of Figure 1 nevertheless reveal that these differences were not present at the last assessment (36 months) anymore. Patients with second-degree FHPD scored on average 5.84 points lower on the GAF over the 3 years ($F_{(1,240.495)} = 8.455$, $p = .004$).

Finally, several relationships between sociodemographic and clinical variables and the number of relatives with FHPD were highlighted. The total number of first- and second-degree of FHPD was associated with higher SES ($\rho = .102$, $p = .039$) and less frequent migration in adversity ($r = -0.120$, $p = .015$). A higher number of FHPD was also associated with more frequent psychiatric history ($r = -0.142$, $p = .003$), more frequent lifetime alcohol dependence ($r = -0.133$, $p = .008$) and more severe CGI-symptoms at the beginning of the program ($\rho = .158$, $p = .004$). The number of first- and second-degree of FHPD was also associated with less frequent functional recovery (GAF ≥60; $r = -0.153$, $p = .010$) and less frequent work recovery

TABLE 4 Outcome data according to presence of second degree relative with psychiatric disorder.

	No family history	Second degree family history only		95% CI of OR		
	N = 220	*N* = 41	Odds ratio (OR)	LCI	UCI	*p*-Value
Program commitment, % (N)						
Lost from sight	16.0 (24)	3.2 (1)	0.163	0.021	1.261	.082
Symptomatic response at the last assessment of the last year of the program (Andreassen), % (*N*)	53.3 (49)	51.7 (15)	0.953	0.410	2.215	.911
Functional recovery (PAS) at the last assessment of the last year of the program, % (*N*)	50.7 (74)	36.7 (11)	0.614	0.269	1.399	.246
Functional recovery (GAF ≥60), % (*N*)	60.3 (85)	44.1 (15)	0.547	0.254	1.176	.122
Functional recovery—independent work, % (*N*)	36.5 (54)	14.3 (5)	0.270	0.098	0.744	.011
Functional recovery—independent living, % (*N*)	59.9 (88)	48.6 (17)	0.650	0.308	1.370	.258
Combined functional recovery (indep. work & living), % (*N*)	27.9 (41)	11.4 (4)	0.321	0.106	0.973	.045

Note: All analyses were adjusted for SES.
Abbreviation: Ref. cat., reference category.

($r = -.165$, $p = .004$) at the end of the programme. Finally, patients with higher number of FHPD were less likely to disengage from the programme ($r = -0.129$, $p = .028$).

4 | DISCUSSION

The aim of this study was to study the impact of a family history of psychiatric disorders (FHPD) on the characteristics of early psychosis patients in a specialized programme. Our results globally highlighted a relationship between FHPD and less favourable characteristics of patients presenting a first episode of psychosis.

In our sample, we found a high prevalence of FHPD. Indeed, about half of the patients had a FHPD and in about one third a first degree relative was concerned. Considering the potential considerable impact of mental health disorders on family members and family dynamics, this issue should be explored in each first episode psychosis patient in order to provide the support that may be needed.

Patients with first degree FHPD were more likely to have been exposed to trauma and less likely to have experienced migration in adversity. They were more likely to suffer from alcohol abuse and showed a higher CGI score at presentation. No significant impact on outcome was highlighted. Our observation that first degree FHPD was associated with more frequent trauma need to be interpreted with caution. Although it may be in phase with the idea that parents with psychiatric disorder need support in raising their children, it is also possible that children of parents with psychiatric disorders may be more vulnerable to other forms of trauma. Whatever the case may be, this suggests that programs aimed at providing support to parents with a psychiatric disorder are very important and need to be developed. For instance, the PRIMERA (Promoting Research and Innovation in Mental hEalth seRvices for fAmilies and Children) research programme has been developed. It aims to identify, help implement and evaluate family-focused interventions for families where a parent has a mental illness. This programme also highlighted a clear recognition of the importance of this work among professionals and a commitment to address the needs of these vulnerable families (Furlong et al., 2021). The fact that prevalence of alcohol abuse was more prevalent in this subgroup may as well be linked to a contextual effect; indeed, most patients report using substances in order to avoid negative feelings (Gregg et al., 2007) and this may be the case in this subgroup of patients as well. We also found that patients with first degree FHPD were less likely to have a migration history is in phase with our previous observation that psychosis in migrant populations is more likely to be linked to history of trauma than to genetically and inherited pathways (Golay et al., 2019). It is nevertheless important to note that information on FHPD may be less accurate for patients who have migrated in adverse context, as they may not be fully aware of family diagnoses if they could even be determined in the country of origin.

Patients with second degree FHPD were more likely to suffer from alcohol dependence, had more negative and depressive symptoms over time and poorer functional outcome. They were less likely to attain work-related functional recovery and combined work and independent living recovery at the end of the programme. Our study tended to show that patients with first-degree FHPD had a milder picture overall in term of outcome. While this finding is not intuitive nor easily explainable, it must be counterbalanced by some of our other results. The total number of parents with FHPD was negatively associated with several clinical variables, suggesting a genetic dose–response relationship. This result implies that familial genetics likely influence the characteristics and evolution of patients with early psychosis. Following this hypothesis, one can ask why patients with first-degree-FHPD did not present a more severe situation than patients with second-degree FHPD only. There are probably many other contextual, relational, and environmental factors interacting in complex ways that determine the influence of FHPD on the course of psychosis. We can hypothesize that patients with first-degree

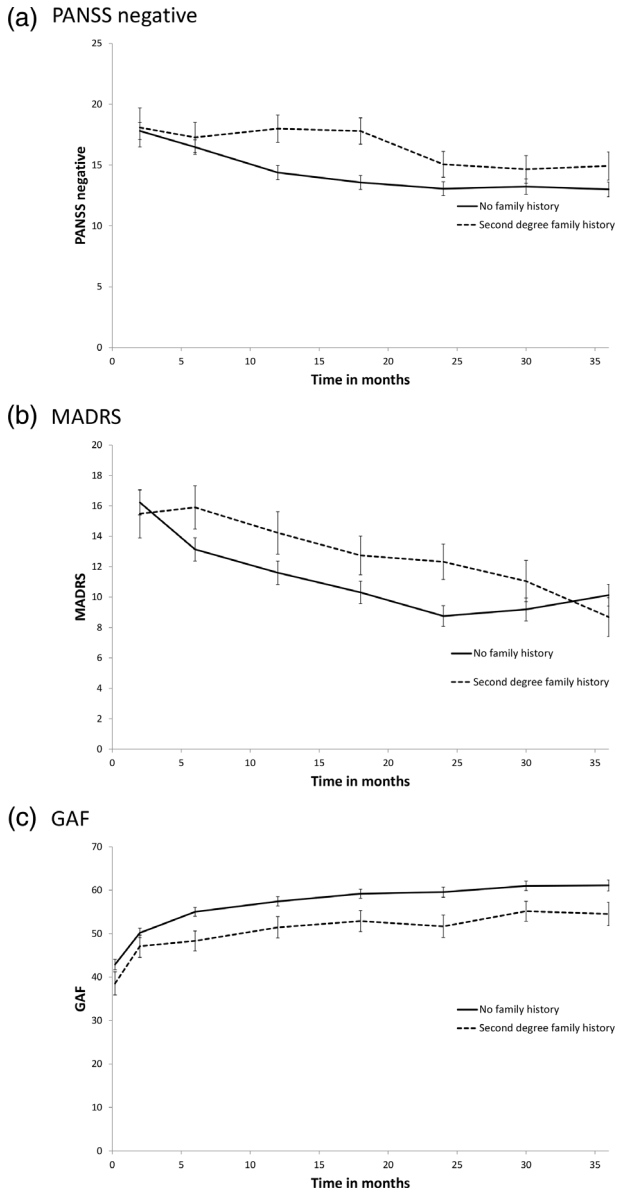

FIGURE 1 Comparison between patients with or without second degree family history of psychiatric disorders over the 3 years of follow-up.

FHPD positively benefitted from the experience of close relatives that facilitated access to care. Indeed, FHPD was also associated with several favourable characteristics like lower programme disengagement and higher socio-economic status. We have no straightforward alternative explanation for a higher SES other than higher access to care which would results in better knowledge and report of FHPD.

In carrying out this research, we were confronted with various other limitations. First, information about FHPD is not always accurate even without a context of migration. Indeed, patients do not necessarily know their family history or diagnoses have not always been made. Secondly, we investigated the impact of FHPD in general, but did not distinguish according to the parents' disorder. It is likely that a family history of psychotic disorder does not have the same impact as a family history of non-psychotic disorder. This distinction should be investigated in future studies. Thirdly, multiple separate statistical analyses were performed in the present study, increasing the risk of false positive results. Correction for different hypothesis-driven tests were not indicated in this instance because we did not have a universal null hypothesis predicting no difference across all variables of the different analysis performed. As a result, the risk of type one error must be borne in mind when interpreting the associations identified. Finally, although FHPD likely influences psychoses, family relationships likely play a significant role in the various characteristics we studied. It would be relevant to analyse their influence in much more detail, considering which family members were specifically affected by psychiatric disorders.

5 | CONCLUSION

The various finding described above suggest the existence of a distinct profile and a more unfavourable disease course in patients with FHPD. This implies that the presence of a FHPD should lead clinicians to explore various aspects of patients' situations (substance abuse, past exposure to trauma, risk of enduring depressive and negative symptoms), in order to improve outcome. Although this is true for all patients, special care should be paid to the way family members are included in treatment, in order to provide the support they may need in order to offer the best context for the recovery process to occur.

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CONFLICT OF INTEREST STATEMENT

PC is an Editorial Board member of Early Intervention in Psychiatry and a co-author of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication. The authors declare that they have no other competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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