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Grouping affective psychoses in early intervention: Justification for specific treatment guidelines

Julie Ramain [a,*], Philippe Conus [a], Philippe Golay [a,b]

[a] Service of General Psychiatry, Treatment and Early Intervention in Psychosis Program (TIPP-Lausanne), Lausanne University Hospital and University of Lausanne, Place Chauderon 18, Lausanne 1003, Switzerland
[b] Institute of Psychology, Faculty of Social and Political Sciences, University of Lausanne, Place Chauderon 18, Lausanne 1003, Switzerland

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ABSTRACT

The concept of affective psychosis regroups psychotic disorders with mood syndrome. Previous studies provided evidence to support a dichotomy between affective and non-affective psychoses although questions remain regarding the utility and validity of such a category to develop clinical guidelines.

The aim of this study is to explore similarities and differences within affective psychoses to question whether strategies would apply to all the diagnoses falling under this umbrella term.

Using Bayesian model comparison methods, we explored the homogeneity of the characteristics of first-episode affective patients ($N = 77$) treated in a specialized 3-year early intervention in psychosis programme.

Our analysis revealed affective psychoses display many similarities regarding socio-demographic variables, the course of positive and manic symptoms over three years, and outcome at discharge. Our results did not support the heterogeneous model. However, despite no significant differences in the course of symptoms with the major depressive disorder group, the schizoaffective disorder group displayed a more severe clinical picture at the beginning of the programme and a poorer functional outcome than the two other groups.

Absence of clear boundaries and the several similarities within affective psychoses suggest they can usefully be grouped to define treatment strategies that are easily legible by clinicians.

1. Introduction

Affective psychosis is a concept applied in both clinical and research settings that groups various psychotic disorders associated with mood syndrome including bipolar disorder I with psychotic features (BD), major depression with psychotic features (MDP), and schizoaffective disorder (SAD; Kraepelin, 1992; Lambert et al., 2003). Affective psychoses remain largely neglected in early intervention strategies and research (Chia et al., 2019; Conus and McGorry, 2002) despite poor functional outcome (Conus et al., 2006). However, the question of the clinical relevance of this concept in addition to DSM or CIM categorical diagnoses remains debated. While some studies reported results for affective psychoses taken as a group (Conus and McGorry, 2002; Husted et al., 1995), and provided guidelines for the treatment of first-episode affective psychoses (Lambert et al., 2003), others focused specifically on BD (Jauhar et al., 2019), SAD (Malhi et al., 2008), or MDP (Rothschild, 2013; Schatzberg, 2003). In addition, a previous publication suggested that in first-episode mania with psychotic features, a distinction between BD and SAD was relevant on the basis of differences in negative symptoms levels and outcome (Conus et al., 2010). However, these previous papers studying the diagnostic categories separately also pointed out to commonalities and overlaps (regarding course of illness or indicated pharmacological treatment) which add support to the hypothesis that recommendations for affective psychoses as a group could be usefully developed. Moreover, the complexity of the concept of SAD makes such distinction challenging considering its overlaps with both schizophrenia and BD (Jäger et al., 2011), as well as its low diagnostic stability and inter-rater reliability (Kane, 2010). Further studies are thus required to explore the clinical relevance of the concept of affective psychoses in addition or instead of existing diagnostic categories, especially with regard to the development of early intervention strategies that may need to be different from the ones applied for first-episode schizophrenia spectrum disorders.

Some recent studies showed that a dichotomy between affective and non-affective psychosis was justified on empirical grounds (Ramain et al., 2021a; Reininghaus et al., 2019). Especially, results from a

* Corresponding author.
E-mail address: julie.ramain@chuv.ch (J. Ramain).

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first-episode psychosis cohort showed that such dichotomy was justified by significant differences between affective and non-affective psychosis patients regarding symptom profile and recovery pattern (Ramain et al., 2021a). In addition, based on premorbid characteristics, the affective psychosis grouping may allow the stratification of first-episode sub--groups with specific needs independently of the diagnostic categories (Ramain et al., 2021b). This approach offers a practical way to define clinical approach in the early phase of treatment. To confort the hypothesis that the concept of affective psychosis is a coherent construction and provides an evidence base for the definition of treatment in early intervention, we investigated similarities and differences amongst first-episode affective psychosis patients regarding clinical presentation and outcome.

2. Method

2.1. Sample and procedure

This prospective study examined a cohort of first-episode psychosis patients treated at a specialised early psychosis intervention programme (the Treatment and Early Intervention in Psychosis Programme; TIPP) that has been implemented by Lausanne University Hospital's Department of Psychiatry in 2004 (Baumann et al., 2013; Conus and Bonsack, 2004). Patients entering the programme are aged 18–35, reside in the Lausanne catchment area and have crossed the psychosis threshold in the Comprehensive Assessment of At-Risk Mental States scale's (CAARMS; Yung et al., 2005) *Psychosis Threshold* subscale. Patients are referred to other programmes if they have been on antipsychotic medication for more than six months, have an intoxication-induced or organic brain disease-induced psychosis, or have an intelligence quotient below 70. A psychiatrist and a case manager follow every patient in the programme for three years. The TIPP favours a bio-psycho-social perspective and provides treatment including psychotherapy, psychoeducation, family support and therapy, cognitive assessment and remediation, social support, supported employment, psychological interventions for cannabis use, and pharmacological treatment. In line with international guidelines, atypical antipsychotics are a first-line pharmacological treatment used to prospectively monitor any side effects (Baumann et al., 2013). Case managers fill out a specifically designed questionnaire for the TIPP with every patient. This includes information about demographic characteristics, medical history, exposure to traumatic life events, symptomatology and functioning. Follow-up assessments are carried out at 2, 6, 12, 18, 24, 30 and 36 months, by a psychologist and a case manager, to explore various aspects of treatment, pharmacotherapy, the psychopathology's evolution, and functional status, as well as co-morbidities (e.g. level of insight, treatment adherence, the presence or absence of a forensic history and substance use, intermittent exposure to trauma, suicide attempts and forensic events). The study was approved by the Human Research Ethics Committee of the Canton of Vaud (protocol #2020–00,272). The data generated during follow-up were only used if patients provided written informed consent; all of them agreed that their clinical data could be used for research, yielding a highly representative sample of early psychosis patients.

2.2. Diagnostic assessment

The diagnoses presented here were the results of an expert consensus built from discussions held at 18 and 36 months, based on the DSM-IV criteria and using information from patients' medical records or hospitalisation reports provided by their treating psychiatrists and their TIPP-assigned psychiatrists and case managers. We used the latest consensus diagnosis available. Patients included in the affective psychoses group were diagnosed with BD, MDP or SAD.

2.3. Socio-demographic and premorbid characteristics

According to the CAARMS criteria, DUP was defined as the time elapsed from the onset of psychosis until admission to TIPP. Socioeconomic status (SES) was subdivided into three categories: low, intermediate and high (Chandola and Jenkinson, 2000). Independent living refers to patients living in independent households, living alone or with friends or family without supervision. The professional activity was subdivided into student or traineeship, active employment, which was defined as partial or full-time job, or other. The premorbid functional level was assessed with the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982) using the childhood and early adolescence sub-scores (MacBeth and Gumley, 2008), and the total score. We considered that patients had a history of trauma if they had experienced at least one instance of sexual or physical abuse before the onset of psychosis (Alameda et al., 2015, 2016). We defined migration in adversity as migration occurring in adverse contexts (e.g. seeking protection for political reasons, threat of death, exposure to war or extreme poverty). Past psychiatric and substance abuse or dependence diagnoses were evaluated with DSM-IV criteria (American Psychiatric Association, 1994), and past suicide attempts with the ICD-10 classification (Dilling and Dittmann, 1990). Forensic history included all types of offenses. Insight was rated by the case manager as being absent, partial, or full regarding awareness of illness and necessity of treatment.

2.4. Medication, symptomatic and functioning data

Medication was reported by case-managers at 2, 6, 12, 18, 24, 30, 36 months follow-up. The functional level at baseline was assessed with the Social and Occupational Functioning Assessment Scale (SOFAS; American Psychiatric Association, 1994) and the Global Assessment of Functioning (GAF; American Psychiatric Association, 1994). While the SOFAS focuses on social and occupational levels, the GAF also includes the impact of symptomatology. General, psychotic, depressive, and manic symptoms were assessed at 2, 6, 12, 18, 24, 30, 36 months follow-up. General and psychotic symptoms were assessed using the general, positive, and negative symptom subscales of the Positive and Negative Psychotic Syndrome Scale (PANSS; Kay et al., 1987). We measured the severity of depressive symptoms using the Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979), and manic symptoms with the Young Mania Rating scale (YMRS; Young et al., 1978). As the YMRS, MADRS and PANSS scores were not available at baseline in our data, we used the assessment at 2 months as a measure of the level of symptoms at the beginning of the programme.

2.5. Outcomes at discharge

We assessed quality of life at discharge with the World Health Organization Quality Of Life scale (1995). It measures satisfaction with life and self-esteem through 26 self-rated items with 5-point Likert scales ranging from 1 (low satisfaction) to 5 (high satisfaction). We defined symptom recovery as significant improvement of psychotic symptoms at one time after a first-episode of psychosis. We used 8 items of the PANSS (delusion, unusual thought content, hallucinatory behaviour, conceptual disorganization, mannerisms, blunted affect, social withdrawal, lack of spontaneity; Andreasen et al., 2005) following Andreasen's Criteria (score $\leq$ 3) to determine symptomatic recovery. A PAS score equal or lower to the premorbid rating on four of the five PAS general scale's items defined functional recovery (Strakowski et al., 1998). The assessment of independent living recovery (head of household/living alone, with partner, or with peers/living with family with minimal supervision) was carried out using the Modified Vocational Status Index (MVSI) and working recovery (paid or unpaid full- or part-time employment/being an active student in school or university/head of household with employed partner (homemaker/full or part-time

volunteer) using the Modified Location Code Index Independent living (MLCI; Tohen et al., 2000). Insight recovery was defined as full insight at discharge.

2.6. Statistical analysis

We compared the three affective psychosis diagnostic sub-groups (SAD, BD and MDP) using a Bayesian approach which represents an elegant alternative to the classic problem of multiple comparisons and allows evaluating the support for the null hypothesis (Golay et al., 2020, 2019b; Noël, 2015). All 6 possible models were estimated. The first model was the homogeneous model (1, 2, 3) stating that groups (SAD, BD, MDP) did not differ and were issued from the same distribution. It corresponds to the null hypothesis in the classical statistical testing framework. Another model was the heterogeneous model (1), (2), (3) (i.e. all the groups are different from each other and issued from a different distribution; i.e. (SAD), (BD), (MDP)). All other possible combinations, which adds up to 5 — that is (1, 2), (3) or (1), (2, 3) or (1, 3), (2) were also estimated. For continuous variables, the best possible Gaussian model (μ, σ2) was determined by using the Bayesian information criterion (Schwarz, 1978). For nominal variables, the best multinomial model was determined using the exact likelihood with a uniform prior on all parameters (Noël, 2015). An equal prior probability of 1/5 was assumed for all models so that no model was favoured. The Bayes factor was also computed (Kass and Raftery, 1995) and provided a comparison between the best model and the homogenous model. A Bayes factor of 4 indicates that the best model was 4 times more likely to be true than the homogenous model. Values over 3 are generally considered sufficiently important to favour one model over another (Jeffreys, 1961; Wagenmakers et al., 2011). The course of symptoms (general, positive, negative, depressive, manic) and functioning over time were compared between the SAD, BD, and MDP groups using mixed effects models repeated measures analysis of variance (MMRM). In these models, the "within-group" factor was time and the "between-groups" factor was the diagnostic group. From the model, the main effects of the groups and time can be examined as well as their interaction. Main effects were examined only if the interaction term was not significant. We selected the optimal within-subject covariance matrix in each MMRM with the Akaike Information Criterion (AIC) coefficient. All the analyses were performed with IBM SPSS statistics 26, the AtelieR package for R (Noël, 2013) and the Bayes R2STATS group models online calculator (Noël, 2018).

Table 1
Comparison of socio-demographic and premorbid characteristics between diagnostic categories within affective psychoses.

	(1) Schizoaffective disorder (n = 35)	(2) Major depression with psychotic features (n = 16)	(3) Bipolar disorder (n =26)	Best Model[a]	Bayes factor against null hypothesis[b]	Probability of the model to be true[c]
Sex, % males (n)	**51.4 (18)**	**43.8 (7)**	**53.8 (14)**	**(1, 2, 3)**	**1.0000**	**0.4699**
Age, M (SD)	**25.17 (4.61)**	**25.38 (5.20)**	**25.12 (5.08)**	**(1, 2, 3)**	**1.0000**	**0.7367**
Level of education, M (SD)	**10.39 (2.32)**	**9.67 (2.87)**	**11.19 (2.64)**	**(1, 2, 3)**	**1.0000**	**0.5326**
SES, % (n)				(1, 3), (2)	2.7479	0.4916
Low	20.0 (7)	25.0 (4)	15.4 (4)			
Medium	42.9 (15)	62.5 (10)	30.8 (8)			
High	37.1 (13)	12.5 (2)	53.8 (14)			
Marital status, % (n)				**(1, 2, 3)**	**1.0000**	**0.5017**
Single	76.5 (26)	62.5 (10)	96.2 (25)			
Maried	11.8 (4)	31.3 (5)	0.0 (0)			
Divorced	5.9 (2)	6.3 (1)	3.8 (1)			
Cohabitation	5.9 (2)	0.0 (0)	0.0 (0)			
Professional activity, % (n)				(1, 2), (3)	1400.9766	0.7543
Active employment	8.8 (3)	12.5 (2)	33.3 (8)			
Student/traineeship	11.8 (4)	25.0 (4)	45.8 (11)			
Others	79.4 (27)	62.5 (10)	20.8 (5)			
Life style, % (n)				(1, 3), (2)	1.7265	0.4383
Independent	73.5 (25)	50.0 (8)	76.0 (19)			
Others	26.5 (9)	50.0 (8)	24.0 (6)			
DUP[d], Mdn (IQR)	**67.00 (254.00)**	**65.50 (153.00)**	**23.50 (69.75)**	**(1, 2, 3)**	**1.0000**	**0.5277**
Suicide, % (n)	17.6 (6)	25.0 (4)	3.8 (1)	(1, 2), (3)	1.1991	0.3434
Trauma, % (n)	**29.4 (10)**	**25.0 (4)**	**23.1 (6)**	**(1, 2, 3)**	**1.0000**	**0.5093**
Migration in adversity, % (n)	42.9 (15)	37.5 (6)	19.2 (5)	(1, 2), (3)	1.7126	0.3774
Forensic history, % (n)	24.1 (7)	6.7 (1)	0.0 (0)	(1), (2, 3)	5.8453	0.5464
Psychiatric antecedents, % (n)	60.0 (21)	37.5 (6)	42.3 (11)	(1), (2, 3)	1.1606	0.3214
Familial psychiatric history, % (n)	64.7 (22)	42.9 (6)	64.0 (16)	(1, 3), (2)	1.0034	0.3353
Substance abuse, % (n)	**14.7 (5)**	**6.3 (1)**	**7.7 (2)**	**(1, 2, 3)**	**1.0000**	**0.5570**
Dependence to substance, % (n)	**11.8 (4)**	**0.0 (0)**	**7.7 (2)**	**(1, 2, 3)**	**1.0000**	**0.5443**
Insight, % (n)				(1, 3), (2)	36.3186	0.7463
Null	44.1 (15)	12.5 (2)	30.8 (8)			
Partial	32.4 (11)	81.3 (13)	34.6 (9)			
Full	23.5 (8)	6.3 (1)	34.6 (9)			
PAS childhood, M (SD)	**0.29 (0.21)**	**0.25 (0.16)**	**0.24 (0.19)**	**(1, 2, 3)**	**1.0000**	**0.6386**
PAS Early adolescence M (SD)	**0.32 (0.17)**	**0.28 (0.20)**	**0.28 (0.19)**	**(1, 2, 3)**	**1.0000**	**0.6448**

Note. Lines in bold highlight homogeneity between groups. *a* = based on BIC coefficient; *b* = Bayes factor comparing the best model to the homogeneous model (1, 2, 3); *c* = compared to all possible models ((1, 2, 3) / (1, 2) (3) / (1) (2, 3) / (1, 3) (2) / (1) (2) (3)); *d*= Raw data are presented, however the test statistics were based on log10 (+constant) transformed data because of extreme positive skewness.

3. Results

3.1. Patient sample

Our sample consisted of 77 patients (Mean age = 25.19; SD = 4.83) who met diagnostic criteria for affective psychosis (33.8% BD, 20.8% MDP, 45.5% SAD) Table 1.

3.2. Socio-demographic and premorbid characteristics (Table 1)

Results showed that BD, MDP and SAD patients were similar regarding gender repartition, age, level of education as well as marital status. The DUP was also similar in all categories. Considering their past history, all groups displayed a similar prevalence of exposure to trauma, substance abuse and dependence. They were also similar regarding their functional level during adolescence and childhood.

MDP patients were less likely than the two other groups to have high SES, to live independently, to have a family history of psychiatric disorder and to display full insight at baseline.

Patients with BD were more likely to have an active professional/training activity at baseline and were less likely to have a past history of suicide or migration in adversity than patients with SAD or MDP.

The SAD group was more likely to have a forensic history and psychiatric antecedents than BD and MDP patients Table 2.

3.3. Clinical presentation at the beginning of the programme (Table 2)

The groups were similar regarding the severity of the positive, manic and general symptomatology at 2 months. The SAD group was more likely to have more severe depressive symptoms at 2 months, as well as a worse level of socio-occupational and symptomatic functioning (SOFAS and GAF scores) at baseline than the two other groups. The BD group was more likely to have less severe negative symptoms at 2 months.

3.4. Course of symptoms and functioning over the 36 months of programme

The course of general and negative symptoms differed significantly between SAD and BD patients over the first 18 months. Indeed, the SAD group had significantly more severe general symptoms (Fig. 1 A.) at 2 (mean difference = 7.056; df = 2.627; $p = 0.011$), 6 (mean difference = 9.142; df = 2.907; $p = 0.003$), 12 (mean difference = 11.450; df = 2.739; $p < 0.001$), 18 (mean difference = 8.492; df = 3.521; $p = 0.021$) months than the BD group. The SAD group had also significantly greater severity of negative symptomatology at 2 (mean difference = 6.731; df = 1.840; $p < .001$), 6 (mean difference = 4.957; df = 1.824; $p = 0.007$), 12 (mean difference = 4.995; df = 1.874; $p = .008$), 18 (mean difference = 5.248; df = 2.181; $p = 0.017$) months than the BD group (Fig. 1 C.).

The SAD group had significantly more severe general symptoms at 12 months (mean difference = 6.493; df = 3.194; $p = 0.048$; Fig. 1 A.) than the MDP group. However, general symptoms were significantly less severe at 36 months in the SAD (mean difference = −7.553; df = 2.622; $p = 0.008$; Fig. 1 A.), and in the BD (mean difference = −7.277; df = 2.872; $p = 0.018$; Fig. 1 A.) groups than in the MDP group. The SAD group had also significantly more negative symptoms than the MDP group at 6 months only (mean difference = 4.462; df = 2.210; $p = .045$; Fig. 1 C.).

The SAD group had significantly more positive psychotic symptoms than the BD groups only at 12 months (mean difference = 3.872; df = 1.355; $p = 0.007$; Fig. 1 B.). The three groups did not significantly differ regarding positive symptoms at any other time point.

The SAD group had more depressive symptoms than the BD group during the first year. Indeed, depressive symptoms were significantly more severe at 2 (mean difference = 9.844; df = 3.592; $p = .007$), 6 (mean difference = 8.949; df = 3.541; $p = .013$), and 12 (mean difference = 8.836; df = 3.757; $p = .020$) months (Fig. 2 A.) in the SAD than in the BD group. The SAD group and the MDP group did not differ significantly regarding depressive symptoms until the 36 months with more severe in the MDP group (mean difference = 9.380; df = 4.647; $p = .045$; Fig. 2 A.). All the groups did not differ significantly at any time point regarding manic symptoms (Fig. 2 B.).

The SAD group had poorer functioning (SOFAS scores) than the BD group at baseline (mean difference = −10.833; df = 4.547; $p = .020$), 2 (mean difference = −11.355; df = 4.080; $p = .007$), 12 (mean difference = −13.769; df = 3.868; $p = .001$), 18 (mean difference = −13.051; df = 3.283; $p = .000$), 24 (mean difference = −8.889; df = 4.154; $p = .036$), 30 (mean difference = −10.450; df = 4.139; $p = .014$) months (Fig. 3). The SAD group had also poorer functioning than the MDP group at 18 (mean difference = −12.331; df = 3.622; $p = .001$), 24 (mean difference = −12.800; df = 4.621; $p = .007$), and 30 (mean difference = −10.840; df = 4.907; $p = .030$) months (Fig. 3). Results were globally similar with the GAF scores Table 3.

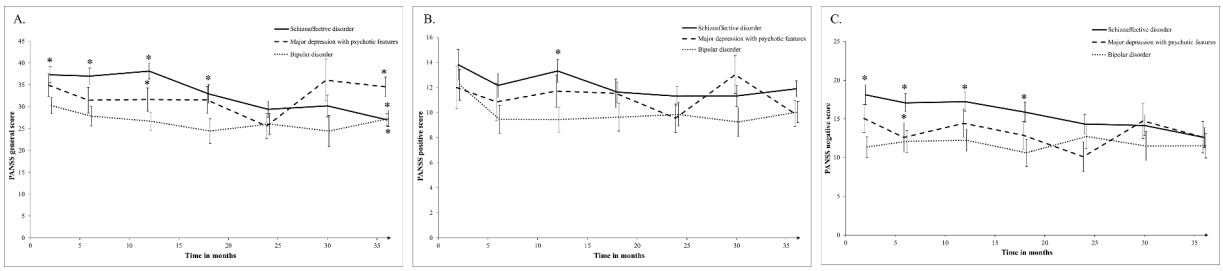
3.5. Medication over the 36 months of programme (Table 3)

Medication was similar in the three diagnostic groups at 12 months. Medication of the MDP group differed from the two other groups at 2, 18, and 36 months. Medication of the SAD group was different from the

Table 2
Comparison of clinical data between diagnostic categories within affective psychoses at the beginning of the programme.

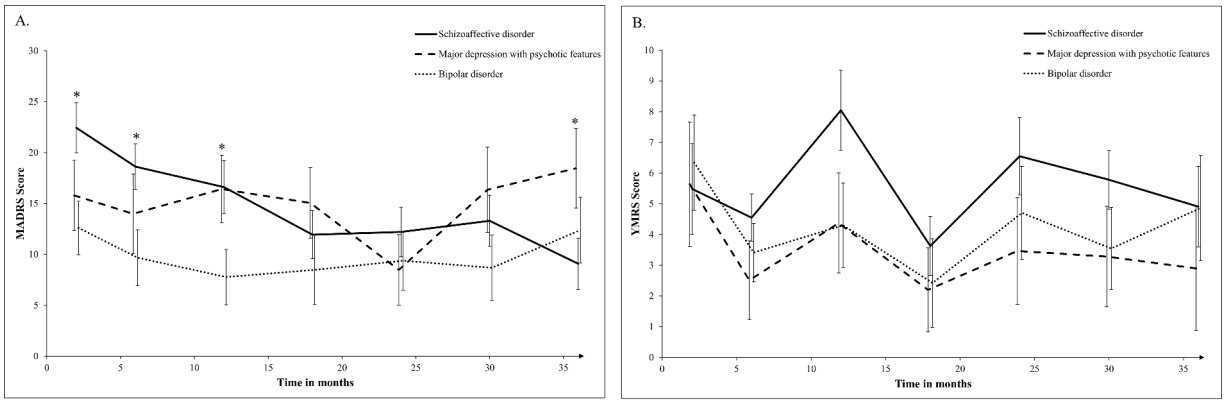
	(1) Schizoaffective disorder (n = 35)	(2) Major depression with psychotic features (n = 16)	(3) Bipolar disorder (n = 26)	Best Model[a]	Bayes factor against null hypothesis [b]	Probability of the model to be true[c]
2 months PANSS positive, M (SD)	**13.33 (4.42)**	**12.00 (3.92)**	**12.31 (4.52)**	**(1, 2, 3)**	**1.0000**	**0.6029**
2 months PANSS negative, M (SD)	17.75 (5.77)	15.14 (4.22)	12.46 (4.31)	(1, 2), (3)	3.2269	0.3766
2 months PANSS general, M (SD)	**36.50 (6.75)**	**34.57 (7.28)**	**31.61 (6.63)**	**(1, 2, 3)**	**1.0000**	**0.3627**
2 months MADRS, M (SD)	22.17 (13.25)	16.14 (7.84)	12.75 (9.62)	(1), (2, 3)	1.4780	0.3789
2 months YMRS, M (SD)	**5.42 (5.70)**	**6.14 (5.27)**	**6.50 (5.35)**	**(1, 2, 3)**	**1.0000**	**0.6186**
Baseline GAF, M (SD)	35.70 (13.07)	47.07 (17.96)	46.88 (22.37)	(1), (2, 3)	4.1898	0.6474
Baseline SOFAS, M (SD)	36.62 (12.04)	48.13 (16.98)	47.71 (19.88)	(1), (2, 3)	9.6283	0.7560

Note. Lines in bold highlight homogeneity between groups *a* = based on BIC coefficient; *b* = Bayes factor comparing the best model to the homogeneous model (1, 2, 3); *c* = compared to all possible models ((1, 2, 3) / (1, 2) (3) / (1) (2, 3) / (1, 3) (2) / (1) (2) (3)).



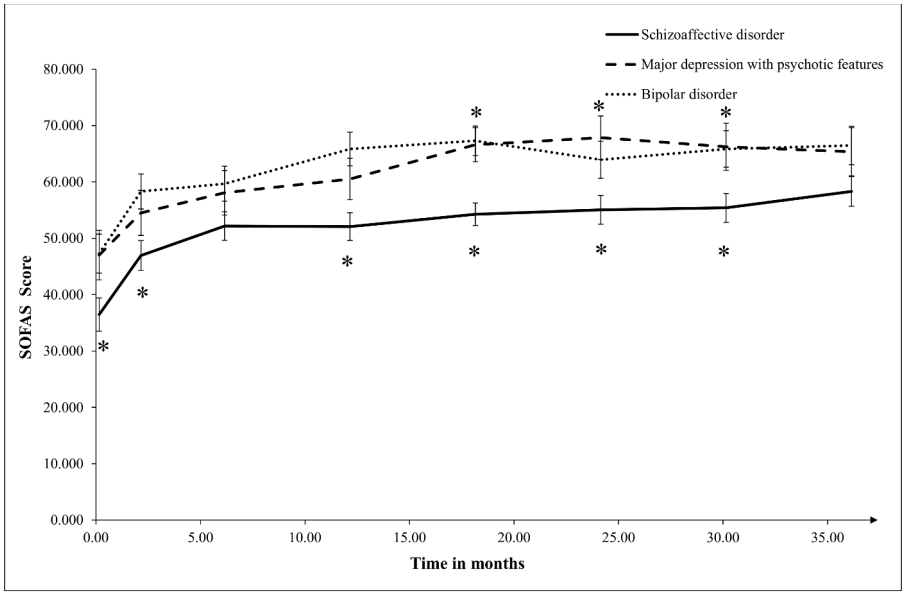
Note. *p<.05

Fig. 1. The course of general (A), positive (B), and negative (C) symptoms of schizoaffective disorder, major depression with psychotic features, and bipolar disorder over the 36 months of the programme.
Note. *p<.05.



Note. *p<.05

Fig. 2. The course of depressive (A) and manic (B) symptoms of schizoaffective disorder, major depression with psychotic features, and bipolar disorder over the 36 months of the programme.
Note. *p<.05.



Note. *p<.05

Fig. 3. The course of functioning of schizoaffective disorder, major depression with psychotic features, and bipolar disorder over the 36 months of the programme.
Note. *p<.05.

Table 3
Comparison of medication between diagnostic categories within affective psychoses.

	(1) Schizoaffective disorder (n = 35)	(2) Major depression with psychotic features (n = 16)	(3) Bipolar disorder (n = 26)	Best Model[a]	Bayes factor against null hypothesis [b]	Probability of the model to be true[c]
Medication, 2 months % (n)				(1, 3), (2)	1.4375	0.2820
Antipsychotic	80.0 (8)	55.6 (5)	50.0 (3)			
Mood stabilizer	0.0 (0)	0.0 (0)	16.7 (1)			
Antipsychotic & mood stabilizer	20.0 (2)	0.0 (0)	16.7 (1)			
Antipsychotic & antidepressant	0.0 (0)	44.4 (4)	16.7 (1)			
Medication, 6 months % (n)				(1), (2, 3)	7.0205	0.4408
Antipsychotic	61.5 (8)	28.6 (2)	14.3 (1)			
Antidepressant	0.0 (0)	14.3 (1)	14.3 (1)			
Mood stabilizer	0.0 (0)	0.0 (0)	14.3 (1)			
Antipsychotic & mood stabilizer	30.8 (4)	0.0 (0)	14.3 (1)			
Antipsychotic & antidepressant	7.7 (1)	57.1 (0)	28.6 (2)			
Antidepressant & mood stabilizer	0.0 (0)	0.0 (0)	14.3 (1)			
Medication, 12 months % (n)				**(1, 2, 3)**	**1.0000**	**0.3121**
Antipsychotic	38.5 (5)	25.0 (2)	20.0 (1)			
Antidepressant	7.7 (1)	0.0 (0)	0.0 (0)			
Mood stabilizer	7.7 (1)	0.0 (0)	40.0 (2)			
Antipsychotic & mood stabilizer	15.4 (2)	0.0 (0)	0.0 (0)			
Antipsychotic & antidepressant	23.1 (3)	75.0 (6)	40.0 (0)			
Antidepressant & mood stabilizer	7.7 (1)	0.0 (0)	0.0 (0)			
Medication, 18 months % (n)				(1, 3), (2)	44.7853	0.4642
Antipsychotic	50.0 (7)	0.0 (0)	14.3 (0)			
Antidepressant	0.0 (0)	42.9 (3)	0.0 (0)			
Sedative	7.1 (1)	14.3 (1)	0.0 (0)			
Mood stabilizer	7.1 (1)	0.0 (0)	42.9 (3)			
Antipsychotic & mood stabilizer	14.3 (2)	0.0 (0)	14.3 (1)			
Antipsychotic & antidepressant	14.3 (2)	42.9 (3)	28.6 (2)			
Antipsychotic, antidepressant & mood stabilizer	7.1 (1)	0.0 (0)	0.0 (0)			
Medication, 24 months % (n)				(1), (2), (3)	2.3188	0.2869
Antipsychotic	44.4 (8)	33.3 (1)	22.2 (2)			
Sedative	5.6 (1)	0.0 (0)	0.0 (0)			
Mood stabilizer	5.6 (1)	0.0 (0)	44.4 (4)			
Antipsychotic & mood stabilizer	33.3 (6)	0.0 (0)	22.2 (2)			
Antipsychotic & antidepressant	11.1 (2)	66.7 (2)	11.1 (1)			
Medication, 30 months % (n)				(1), (2), (3)	69.7438	0.6581
Antipsychotic	55.6 (10)	25.0 (1)	10.0 (1)			
Mood stabilizer	5.6 (1)	0.0 (0)	40.0 (4)			
Antipsychotic & mood stabilizer	33.3 (6)	0.0 (0)	30.0 (3)			
Antipsychotic & antidepressant	5.6 (1)	75.0 (3)	20.0 (2)			
Medication, 36 months % (n)				(1, 3), (2)	26.2083	0.6005
Antipsychotic	50.0 (8)	20.0 (1)	30.0 (3)			
Antidepressant	0.0 (0)	60.0 (3)	0.0 (0)			
Sedative	12.5 (2)	0.0 (0)	0.0 (0)			
Mood stabilizer	6.3 (1)	0.0 (0)	40.0 (4)			
Stimulant	6.3 (1)	0.0 (0)	0.0 (0)			
Antipsychotic & mood stabilizer	18.8 (3)	0.0 (0)	20.0 (2)			
Antipsychotic & antidepressant	6.3 (1)	20.0 (1)	10.0 (1)			

Note. *a* = based on BIC coefficient; *b* = Bayes factor comparing the best model to the homogeneous model (1, 2, 3); *c* = compared to all possible models ((1, 2, 3) / (1, 2) (3) / (1) (2, 3) / (1, 3) (2) / (1) (2) (3)).

Table 4
Comparison of outcomes between diagnostic categories within affective psychoses.

	(1) Schizoaffective disorder (n = 35)	(2) Major depression with psychotic features (n = 16)	(3) Bipolar disorder (n = 26)	Best Model[a]	Bayes factor against null hypothesis [b]	Probability of the model to be true[c]
Symptomatic recovery, % (n)	31.3 (5)	40.0 (2)	100.0 (10)	(1, 2), (3)	301.5605	0.6128
General functional recovery, % (n)	37.5 (12)	63.6 (7)	70.0 (14)	(1), (2, 3)	5.2093	0.4756
Premorbid adjustment recovery, % (n)	**40.0 (8)**	**50.0 (4)**	**64.3 (9)**	**(1, 2, 3)**	**1.0000**	**0.2816**
Insight recovery, % (n)	**76.7 (23)**	**63.6 (7)**	**70.6 (12)**	**(1, 2, 3)**	**1.0000**	**0.4279**
Independent living recovery, % (n)	**70.0 (21)**	**83.3 (10)**	**72.2 (13)**	**(1, 2, 3)**	**1.0000**	**0.4488**
Working recovery, % (n)	13.3 (4)	50.0 (6)	44.4 (8)	(1), (2, 3)	14.7333	0.5933
Quality of life, M (SD)						
Quality of physical health	**24.24 (5.58)**	**28.60 (5.03)**	**27.00 (2.83)**	**(1, 2, 3)**	**1.0000**	**0.3313**
Quality of psychological aspects	**21.50 (4.96)**	**22.92 (3.67)**	**21.60 (4.59)**	**(1, 2, 3)**	**1.0000**	**0.5744**
Quality of social relationships	**11.00 (2.13)**	**11.40 (1.67)**	**11.17 (2.40)**	**(1, 2, 3)**	**1.0000**	**0.5893**
Quality of environment	30.83 (6.77)	32.53 (4.32)	36.17 (3.19)	(1, 2), (3)	1.1512	0.3442

Note. Lines in bold highlight homogeneity between groups *a* = based on BIC coefficient; *b* = Bayes factor comparing the best model to the homogeneous model (1, 2, 3); *c* = compared to all possible models ((1, 2, 3) / (1, 2) (3) / (1) (2, 3) / (1, 3) (2) / (1) (2) (3)).

two other groups at 6 months. Medication was different for every diagnostic categories at 24 and 30 months follow-up Table 4.

3.6. Outcomes (Table 4)

All the groups had similar premorbid adjustment, insight and independent living recovery. They also had a similar quality of physical health, psychological aspects, social relationships. Patients with a SAD were less likely to recover functionally and to get back to work than patients of the two other groups. Patients with BD were more likely to achieve symptomatic recovery and to have a better quality of environment than patients of the two other groups.

4. Discussion

Previous studies showed that a dichotomy between affective and non-affective psychoses was empirically justified (Ramain et al., 2021a; Reininghaus et al., 2019), and that the affective psychosis grouping, based on premorbid characteristics and independent of the diagnostic categories, could be used to develop stratification strategies of sub-groups of first-episode patients with specific needs (Ramain et al., 2021b). In order to further explore the relevance of the concept of affective psychosis in early intervention, we studied in the current paper, similarities and differences amongst patients displaying first-episode affective psychosis. In this aim, rather than relying on standard statistical tests that allow only the exclusion of statistical differences, we applied Bayesian statistic methods that permit to explore homogeneity within samples very specifically, and allow to evaluate the statistical support for the null hypothesis. Globally, our results did not support the heterogeneous model of clear differences between every diagnostic category. In addition, our results revealed important similarities amongst SAD, BD and MDP patients regarding socio-demographic variables, premorbid history, clinical presentation at the beginning of the programme, outcomes, as well as no significant differences in the course of positive and manic symptoms. Based on these elements, it seems that there is no clear boundaries between all the three groups, while there are several similarities amongst affective psychosis patients to justify considering them as a group when developing clinical guidelines for early intervention.

Indeed, the heterogeneous model, suggesting clear boundaries between every diagnostic category, was not observed for the premorbid characteristics, the course of symptoms and functioning, neither for the outcomes. Only medication at 24 and 30 months was different for every group. Moreover, all the diagnostic categories were similar regarding many premorbid characteristics that determine outcome (gender repartition, age, level of education, marital status, rate of exposure to trauma, to substance abuse and dependence, and functional level during adolescence). In addition, severity of positive, manic and general symptomatology at 2 months post entry to the programme were similar, suggesting a similar pattern of short-term evolution. Moreover, the course of positive psychotic and manic symptoms did not differ significantly between groups over the 3-year follow-up. In addition, differences between groups regarding the course of depressive, negative, and general symptoms were sparse after 18 months follow-up. Finally, all affective psychosis patients had similar rate of insight development, of return to premorbid adjustment and to independent living at the end of the programme.

However, there were also domains where homogeneity between groups was more limited. In line with previous findings (Conus et al., 2010), SAD patients were the ones displaying the poorest clinical picture. These patients were more likely to have a forensic history and psychiatric antecedents, had more severe depressive symptoms at the beginning of the programme, as well as worse level of functioning than BD and MDP patients. During the first year of the follow-up, they displayed more enduring symptoms than the BD group, which is somewhat understandable considering that the presence of psychotic symptoms for a longer period is at the basis of their clinical definition (American Psychiatric Association, 2013). They also had a poorer functioning than the BD group during the 36 months follow-up. In line with previous findings (Conus et al., 2010; Schöttle et al., 2012), SAD patients were less likely than the two other groups to recover functionally at the end of treatment. The worse functional and professional recovery observed in this group is probably not associated with the course of symptomatology, which globally did not differ between MDP and SAD, but rather with a more severe clinical picture since the beginning. Early intervention in affective psychoses may therefore require more intensive treatment strategies targeting functioning for SAD.

Furthermore, patients with BD were the ones displaying the mildest clinical picture. Indeed, they were more likely to have an active professional/training activity at baseline and were less likely to have attempted suicide before entering the programme and to have a history of migration in adversity than patients with SAD or MDP. They also

displayed the lowest levels of negative symptoms, both at 2 and 36 months. Finally, they were more likely to achieve full symptomatic recovery and to have a better quality of environment than MDP and SAD patients at discharge. The reason for the better outcome we observed in BD patients is probably multi factorial, our observation that they were less likely than the two other groups to have been exposed to migration in adversity might play a role in this regard. Indeed, migration in adversity may increase the risk of exposure to traumatic events and was previously reported to be associated with an increased risk of relapse, as well as with poorer symptomatic remission in first-episode psychosis (Golay et al., 2019a).

Otherwise, our study revealed a strong clinical resemblance between MDP and SAD, especially regarding their clinical presentation at the beginning of the programme, the course of symptoms and outcomes. While various authors have focused on a continuum between BD and schizophrenia, including an intermediate position for SAD, they often did not include MDP in such a dimensional concept (Craddock et al., 2009; Ivleva et al., 2010; Keshavan et al., 2011). In line with Keshavan et al. (2011), and based on our results, we consider indeed this as an argument to include MDP within the large concept of the psychosis spectrum.

In sum, our study shows that there is no clear boundaries between all the affective psychosis diagnostic categories, while there are several similarities within the affective psychosis group. Combined with our previous observation of an affective and non-affective psychoses dichotomy (6), they bring support to the relevance of the affective psychosis concept as a practical way to group patients in order to develop guidelines in early intervention. Reducing the complexity of diagnosis may contribute to promote the development of early intervention strategies that are still largely lacking for affective psychoses (Chia et al., 2019; Conus and McGorry, 2002). This simpler grouping may be a complement to a completely dimensional approach where treatment would be constructed on the presence of each psychopathological domain, which has its limitations (Potuzak et al., 2012).

Our results must be interpreted with caution due to some limitations. First, the sample size is moderate, limiting the power to distinguish between groups. However, this was one motivation to use a Bayesian model comparison approach that partly circumvent the Type I and Type II error trade-off. However, the Bayesian approach was not directly applicable for the MMRM longitudinal modelling. Secondly, our data did not allow us to compare patients on the basis of symptomatic baseline presentation.

5. Conclusion

Our study revealed no clear boundaries and similar clinical features between schizoaffective disorder, major depressive disorder and bipolar disorder with psychotic features. The concept of affective psychoses may therefore be clinically relevant in order to develop treatment guidelines. Patients with schizoaffective disorder may however require more intensive care to improve functioning. In spite of this, it seems justified to conduct studies designed to explore the impact of interventions specifically developed for early affective psychoses as a group.

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CRediT authorship contribution statement

Julie Ramain: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft. **Philippe Conus:** Conceptualization, Funding acquisition, Writing – review & editing. **Philippe Golay:** Conceptualization, Formal analysis, Methodology, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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