Exploring the clinical relevance of a dichotomy between affective and non-affective psychosis: results from a first episode psychosis cohort study

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Running title: Affective and non-affective psychosis dichotomy

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Abstract

Aim: Defining diagnosis is complex in early psychosis, which may delay the introduction of an appropriate treatment. The dichotomy of affective and non-affective psychosis is used in clinical setting but lacks scientific basis. In this study, we explore the clinical relevance of this dichotomy on the basis of clinical variables in a sample of first episode psychosis patients.

Method: We conducted a prospective study in a sample of 330 first episode psychosis treated at an early intervention program. Affective and non-affective psychosis patients were compared on premorbid history, baseline data, outcomes and course of symptoms over the three years of treatment.

Results: Affective psychosis patients (22.42%) were more likely to be female, and had a shorter duration of untreated psychosis. The longitudinal analyses revealed that positive symptoms remained higher over the entire follow-up in the non-affective sub-group. A higher degree of variability of manic symptoms and a significantly better insight after 6 months were observed in the affective sub-group. No difference were observed regarding depressive and negative symptoms. At discharge, only the environmental quality of life and insight recovery were better in affective psychosis.

Conclusions: Our study suggests that despite marginal differences at baseline presentation, these sub-groups differ regarding outcome, which may require differentiation of treatment and supports the utility of this dichotomy.

Key words: early medical intervention, mood disorders, patient outcome assessment, psychotic disorders, symptom assessment

1. Introduction

Affective and non-affective psychoses are nosological entities derived from Kraepelin's dichotomy (Kraepelin, 1992) between schizophrenia (dementia preacox) and psychotic mood disorders (manic-depressive insanity). Although understudied (Chia et al., 2019; Conus & McGorry, 2002), affective psychosis is a concept applied in clinical settings referring to forms of psychoses marked by a severe disturbance of mood (Kraepelin, 1992; Lambert, Conus, Lambert, & McGorry, 2003). It has emerged as a way to stratify patients on the basis of clinical presentation, grouping bipolar disorder with psychotic features, major depression with psychotic features and schizoaffective disorder as "affective psychoses", schizophrenia and schizophreniform disorders as non-affective psychoses (Lambert et al., 2003). In order to provide early intervention adjusted to the specificities of psychotic disorders, this dichotomy is nowadays used in treatment guidelines (Lambert et al., 2003). Indeed, the co-occurrence of mood episodes and psychotic features in affective psychosis may require pharmacotherapy considering both dimensions. However, this dichotomy is mainly based on clinical observations and definitions rather than scientific evidence suggesting the need to further investigate their psychopathological differences.

Although schizophrenia and bipolar disorder have been identified as distinct entities through dichotomous classifications, more and more papers point towards a continuum between both entities with prototypic forms of each disorder at the extremes but a majority of people expressing mixed forms (Keshavan et al., 2011; Thaker, 2008). Such studies highlight the limitations of a categorical classification of mental disorders and the need for a more dimensional concept based on clinico-pathological factors, and especially including longitudinal follow-up (Craddock & Owen, 2007; Keshavan et al., 2011; Thaker, 2008). This way of thinking boundaries between disorders would not only provide a distinction of clinical utility but, would also enable to cluster individuals sharing similar features that do not correspond to the prototypical forms of these disorders (Craddock & Owen, 2007). This point is especially crucial in first episode psychosis as studies highlighted a spectrum of disorders rather than discrete diagnostic entities, making diagnostic categorisation and treatment intervention even trickier due to both blurred boundaries and instability of diagnosis in this phase of illness (Conus et al., 2010; McGorry, 1994; Schimmelmann, Conus, Edwards, McGorry, & Lambert, 2005; Shinn et al.,

2017). Indeed, diagnostic classifications are usually based on studies conducted in chronic samples, and therefore are not well adapted to early phases of disorders (McGorry, 1994; McGorry et al., 1995). Dimensional and longitudinal symptom assessment may thus provide a helpful way of identifying differences between diagnostic groups in the early phase of illness (Arrasate et al., 2014).

Although limited, there is some research data suggesting the existence of factors differing between affective and non-affective psychosis, and that the study of this dichotomy may provide elements to improve early diagnosis accuracy, and thus treatment management (Kapila et al., 2019; Schothorst, Emck, & van Engeland, 2006). First, some authors suggested that distinctive characteristics can be observed at baseline within first episode cohorts. Indeed, previous studies suggest that patients with affective psychosis were more likely to be women, had a higher level of education, were less likely to be single, had a shorter duration of untreated psychosis (DUP), an older age at onset, were less likely to attempt suicide, were more likely to have a past history of psychiatric disorder and substance use, and had a better premorbid functioning and adjustment (Conus, Cotton, Schimmelmann, McGorry, & Lambert, 2007; Kapila et al., 2019; Schothorst et al., 2006). Second, regarding psychopathological features, Kapila et al. (2019) pointed out fewer psychotic symptoms, but more manic symptoms in first episode manic psychosis than in schizophrenia spectrum psychosis at baseline. Another naturalistic longitudinal prospective study showed that the affective psychosis sub-group had less negative but more manic symptoms at baseline than the non-affective one (Torrent et al., 2018). At two-year follow-up, these differences had decreased but the affective psychosis sub-group displayed less positive, negative and general symptoms as well as less depressive symptoms. Similarly, Henry et al. (2010) found lower general psychopathology scores and fewer psychotic symptoms after two-year follow-up in affective psychosis. They also highlighted differences in psychotic illness course (episodic vs continuous) which may require specific intervention. Considering recovery, although Banayan, Papetti, Palazzolo, Pringuey, and Darcourt (2007) reported better functioning, symptomatic remission and quality of life at follow-up in the affective psychosis sub-group, they found no difference between sub-groups regarding employment and time living independently.

Considering both the paucity of data and the clinical relevance of the dichotomy between affective and non-affective psychoses in order to guide treatment in the early phase of psychosis, and following the suggestion by Craddock and Owen (2007) we investigated this topic with a longitudinal approach using different symptom dimensions with the following aims : 1) to consolidate previous results regarding baseline characteristics and outcomes differences between affective and non-affective psychoses; (2) to investigate differences between both groups regarding the course of symptoms in the early phase of psychosis.

2. Method

2.1 Sample and procedure

This is a prospective study on a cohort of first episode psychosis patients treated at a specialized early psychosis intervention program, TIPP (Treatment and Early Intervention in Psychosis Program), implemented in Lausanne (Switzerland) since 2004 at the CHUV's Department of Psychiatry (Baumann et al., 2013; P. Conus & Bonsack, 2004). Patients entering the program are aged between 18 and 35, reside in the catchment area of Lausanne and have crossed the psychosis threshold according to the "*Psychosis threshold*" subscale of the Comprehensive Assessment of At Risk Mental States scale (CAARMS; Yung et al., 2005). Patients are directed to other programs if they have been on antipsychotic medication for more than 6 months, an intoxication or an organic brain disease induced psychosis, or if their intelligence quotient is lower than 70. In this program, every patient is followed for 3 years by a psychiatrist and a case manager. The TIPP program favours a bio-psycho-social perspective, and as such provides treatment that includes psychotherapy, psycho-education, 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 first-line pharmacological treatment with a prospective monitoring of any side effects (Baumann et al., 2013). Case managers fill out for every patient a questionnaire specifically designed for the TIPP. This questionnaire gathers information about demographic characteristics, past medical history, exposure to life events, symptomatology and functioning. Follow-up assessments are carried out at 2, 6, 12, 18, 24, 30, and 36 months by a research

psychologist and case managers, exploring various aspects of treatment, evolution of psychopathology and functional level, as well as co-morbidities (e.g. level of insight; treatment adherence; presence or absence of forensic history and substance use; intermittent exposure to trauma; suicide attempts and forensic events). This study was approved by the Human Research Ethics Committee of the Canton Vaud (protocol #2020-00272). The data generated by the follow-up of all patients were used in the study if they provided consent. All of them agreed for their clinical data to be used for research.

2.2 Diagnostic Assessment

Diagnosis results from an expert consensus discussed at 18 and 36 months, based on the DSM-IV criteria using the information from medical or hospitalization reports from treating psychiatrists, as well as from the TIPP-assigned psychiatrist and case manager. We used the latest consensus diagnostic available. Considering potential diagnostic instability in first-episode psychosis cohorts (Gale-Grant et al., 2020), we also examined the diagnostic stability between the first and the latest diagnosis. Patients diagnosed with bipolar disorder, major depression with psychotic features and schizoaffective disorder were included in the affective psychosis group, while those with schizophrenia or other schizophreniform disorders were included in the non-affective psychosis group. Considering the instability of the diagnosis of unspecified psychosis (Cawkwell, Bolton, Karmacharya, Öngür, & Shinn, 2020; Taş, Celik, & Altinbaş, 2019) and its unclear status between affective and non-affective psychoses, these patients were excluded.

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 & Jenkinson, 2000). Independent living refers to patients living in independent households, living alone or with friends or family without supervision. The employment situation 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, Potkin, & Wyatt, 1982) using the childhood and early adolescence sub-scores (MacBeth & 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; Alameda et al., 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 & 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 Symptomatic and functioning data

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. Psychotic, depressive, manic symptoms and insight were assessed at 2, 6, 12, 18, 24, 30, 36 months follow-up. Insight was also measured at baseline. Psychotic symptoms were assessed using the positive and negative symptom subscales of the Positive and Negative Psychotic Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). We measured the severity of depressive symptoms using the Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979), and manic symptoms with the Young Mania Rating scale (YMRS; Young, Biggs, Ziegler, & Meyer, 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 program. Adherence to treatment was repeatedly assessed on a 3-point scale with 1 corresponding to non adherence (0 – 25% of prescribed medication taken), 2 to partial adherence (25-75% of prescribed medication taken) and3 to full adherence (75-100% of prescribed medication taken).

2.5 Outcomes at discharge

We assessed quality of life at discharge with the World Health Organization Quality Of Life scale ("The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World

Health Organization," 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 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 ≤ 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

A series of exploratory logistic regression analyses were conducted with the sub-group affective psychosis (Yes/No) as the dependent variable, and the individual premorbid and baseline variables as predictors (one at a time for each model). We first conducted logistic regression analysis on the main socio-demographic measures (age, gender, SES, DUP) to explore statistical differences between affective and non-affective psychosis and identify control variables. Because the affective and non-affective psychosis differed for gender and DUP, these two variables were also included in the models. The course of symptoms (positive, negative, depressive, manic) and insight over time were compared between sub-groups using exploratory 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 sub-group. From the model, the main effects of affective psychosis 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. We tested for any effect of adherence to treatment during follow-up with Chi-Square tests at each time point. Finally, to assess outcome differences between affective and non-

affective sub-groups, we performed logistic regression. All the analyses were performed with IBM SPSS statistics 25.

3. Results

3.1 Patient sample

Our sample consisted of 368 patients. Patients diagnosed with unspecified psychosis were excluded, yielding a final sample of 330 patients, composed of 74 patients (22.42%) who met diagnostic criteria for affective psychosis (24 with bipolar disorder, 17 with major depression with psychotic features, 33 with schizoaffective disorder) and 256 (77.58%) who met diagnostic criteria for non-affective psychosis (209 with schizophrenia, 47 with schizophreniform disorder). We examined the diagnostic stability over the program, we found that only 2.3% of the patients diagnosed with a non-affective psychosis at 18 months changed to a diagnosis of affective psychosis at 36 months, and none of those diagnosed with an affective psychosis at 18 months changed to a diagnosis of non-affective psychosis at 36 months.

3.2 *Socio-demographic and premorbid characteristics*

Socio-demographic and premorbid characteristics are reported in *Table 1*. There was significantly more females in the affective psychosis group ($p = .008$). Patients with affective psychosis displayed a significantly shorter DUP than non-affective psychosis patients ($p = .002$). No other differences were observed.

Table 1. Sociodemographic and premorbid characteristics of affective and non-affective psychosis

	Total	Affective	Non-affective	OR_a	95% CI of OR_a		p-value
	N =330	N=74 (22.42%)	N=256 (77.58%)		LCI	UCI	
Gender, male % (N)	64.2 (212)	50.0 (37)	68.4 (175)	2.053	1.202	3.506	.008*
Age in year, M (SD)	24.54 (4.687)	25.16 (4.932)	24.32 (4.566)	1.032	.975	1.093	.281
Age of onset, M (SD)	23.12 (5.016)	24.19 (5.090)	22.75 (4.964)	1.030	.974	1.088	.299
Duration of untreated psychosis (days), Mdn (IQR)[a]	93.50 (477.25)	50.00 (181.50)	121.50 (617.25)	.597	.429	.831	.002*
Socio-economical level, % (N)				1.073	.744	1.548	.706
Low	37.3 (123)	37.8 (28)	31.7 (95)				
Intermediate	43.6 (144)	41.9 (31)	44.1 (113)				
High	19.1 (63)	20.3 (15)	48.8 (18)				
Living situation, % (N)				1.196	.670	2.135	.544
Independent	67.8 (217)	67.1 (49)	68.0 (168)				
Others	32.2 (103)	32.9 (24)	32.0 (79)				
Employment situation, % (N)							
Active	14.4 (47)	18.1 (13)	13.4 (34)	Ref.cat	-	-	-
Student/Traineeship	17.8 (58)	26.4 (19)	15.4 (39)	1.293	.543	3.078	.562
Others	67.8 (221)	55.6 (40)	71.3 (181)	.678	.321	1.429	.307
Education in year, M (SD)	10.02 (2.766)	10.48 (2.566)	9.96 (2.804)	1.071	.958	1.198	.228
Marital status, % (N)							
Single	84.0 (272)	78.1 (57)	85.7 (215)	Ref.cat	-	-	-
Married	9.0 (29)	12.3 (9)	8.0 (20)	1.568	.642	3.826	.323
Divorced	3.4 (11)	6.8 (5)	2.4 (6)	2.660	.736	9.609	.136
Cohabitation	3.7 (12)	2.7 (2)	4.0 (10)	.623	.129	3.013	.556
Premorbid adjustment, M (SD)							
Childhood	0.299 (0.187)	0.271 (0.201)	0.306 (0.184)	.426	.078	2.337	.326
Early adolescence	0.319 (0.177)	0.303 (0.183)	0.323 (0.176)	.658	.116	3.734	.637
Total	0.309 (0.171)	0.295 (0.188)	0.313 (0.169)	.668	.102	4.355	.673
Past suicide attempt, % (N)	13.6 (43)	16.4 (12)	12.7 (31)	1.311	.615	2.792	.483
History of trauma[b], % (N)	27.8 (91)	26.8 (19)	28.1 (72)	.847	.456	1.571	.598
Migration in adversity, % (N)	30.9(102)	37.8(28)	28.9(74)	1.481	.845	2.593	.170
Psychiatric history, % (N)	59.9 (194)	50.7 (37)	62.5 (157)	.656	.376	1.143	.137
Familial psychiatric history, % (N)	57.5 (176)	62.9 (44)	55.9 (132)	1.152	.801	1.658	.445
Lifetime substance abuse (DSM-IV), % (N)	53.2 (174)	46.6 (34)	55.1 (140)	.824	.475	1.427	.490
Forensic history, % (N)	13.5 (39)	11.3 (7)	14.1 (32)	.995	.395	2.504	.991

Note. N = total number. M = mean. SD = standard deviation. Mdn = median. IQR = Interquartile range. CI = confidence interval. 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 or sexual abuse. All models were adjusted for gender and duration of untreated psychosis; OR_a = Adjusted odds ratio. Quantitative variables were treated as continuous variables. We used affective psychosis as the reference category of the dependent variable. * p<.05.

3.3 Symptomatic and functional characteristics at the beginning of the program

There was no significant difference between sub-groups regarding symptoms and functioning at entry (*Table 2).*

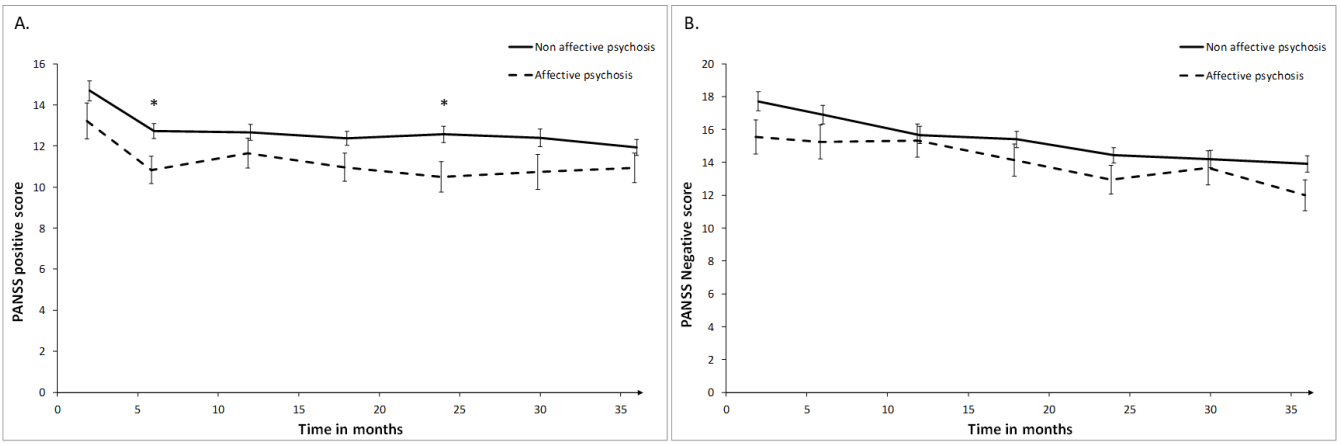
Table 2. Symptomatic and functional characteristics of affective or non-affective psychosis at the beginning of the program

	Total	Affective	Non-affective	OR_a	95% CI of OR_a		p-value
	N =330	N=74 (22.42%)	N=256 (77.58%)		LCI	UCI	
SOFAS at baseline, M (SD)	42.66 (16.171)	42.10 (16.750)	42.30 (16.450)	.998	.982	1.015	.834
GAF at baseline, M (SD)	41.29 (17.159)	41.67 (18.177)	40.74 (17.301)	1.001	.985	1.017	.920
YMRS at the beginning, M (SD)	6.58 (5.805)	6.03 (5.398)	6.83 (6.137)	.973	.904	1.048	.474
MADRS at the beginning, M (SD)	15.91 (9.770)	17.47 (11.404)	15.19 (9.219)	1.029	.985	1.074	.198
PANSS at the beginning, M (SD)							
Positive	13.67 (4.862)	12.77 (4.240)	13.99 (5.158)	.953	.873	1.041	.283
Negative	15.95 (6.070)	15.23 (5.271)	16.54 (6.299)	.966	.899	1.037	.333
General	34.52 (8.162)	34.39 (6.859)	34.61 (8.621)	.994	.945	1.045	.812
Insight at baseline, % (N)				.996	.687	1.443	.983
Full	20.4 (65)	22.5 (16)	19.8 (49)				
Partial	45.8 (146)	42.3 (30)	46.8 (116)				
Null	33.9 (108)	35.2 (25)	33.5 (83)				

Note. N = total number. M = mean. SD = standard deviation. CI = confidence interval. SOFAS, Social and Occupational Functioning Scale; GAF, Global Assessment of Functioning scale; YMRS, Young Mania Rating Scale; MADRS, Montgomery-Asberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale. All models were adjusted for gender and duration of untreated psychosis; OR_a = Adjusted odds ratio. Quantitative variables were treated as continuous variables. We used affective psychosis as the reference category of the dependent variable. * p<.05.

3.4 Clinical course of psychotic, depressive, manic symptoms and insight over time

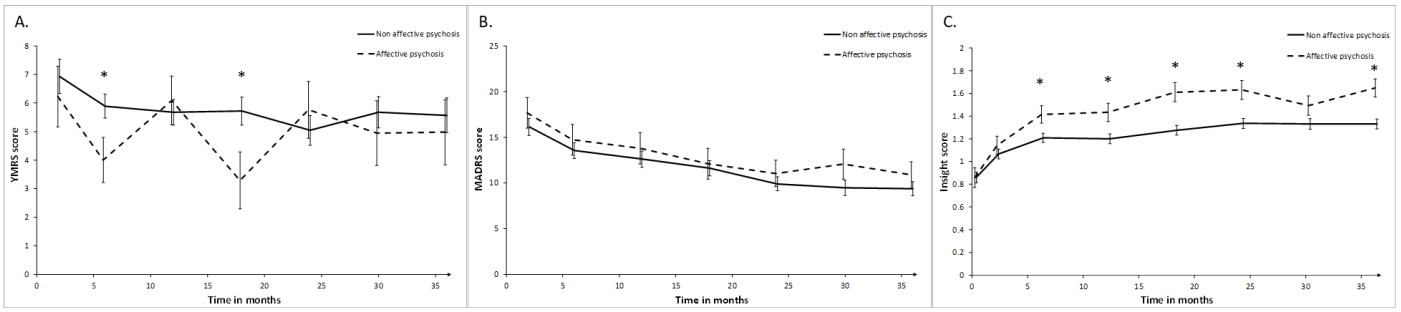
The course of symptoms over time differed between affective and non-affective psychosis. The level of positive symptoms over the three years was significantly higher in the non-affective sub-group (mean difference = 1.502, df = 262.048, p = .006; *Figure 1.A.*). Negative symptoms did not differ significantly (mean difference = 1.339, df = 234.047, p = .068, *Figure 1.B*).



*Note.*p<.05*

Figure 1. Course of positive (A.) and negative (B.) symptoms of affective (N=74) and non-affective psychosis (N=256) across the 36 months follow-up

The variability of manic symptoms over the course of the program was high in the affective psychosis group whereas this dimension remained stable in non-affective psychosis (*Figure 2.A.*). As a result, affective and non-affective psychosis differed both at 6 months (mean difference = 1.887, df = 150.161, p = .037) and at 18 months (mean difference = 2.425, df = 153.553, p = .031) in this regard. The course and level of depressive symptoms (*Figure 2.B.*) did not differ significantly between the sub-groups (mean difference = -1.379, df = 258.234, p = .223). While the level of insight was similar between affective and non-affective psychosis at the beginning of the program, it differed significantly after 6 months (mean difference = -.206, df = .087, p = .019; *Figure 2.C.*), the affective sub-group displaying a higher level of insight. This difference was maintained all along the follow-up. We did not find any significant differences between affective and non-affective psychosis on adherence to treatment at any time point of the follow-up.



*Note.*p<.05*

Figure 2. Course of manic (A.), depressive (B.) symptoms and insight (C.) of affective (N=74) and non-affective psychosis (N=256) across the 36 months follow-up

3.5 Outcome differences at discharge

Results regarding outcome at discharge are reported in *Table 3*. Patients in the affective psychosis sub-group perceived the quality of their environment as better than in the non-affective sub-group (p = .007). Furthermore, patients with affective psychosis had developed a higher level of insight towards the end of the treatment period than those with non-affective psychosis (p = .005). No other significant differences were observed.

Table 3. Outcome differences between affective and non-affective psychosis at discharge

	Affective	Non-affective	OR_a	95% CI of OR_a		p-value
				LCI	UCI	
Quality of life						
Quality of physical health, M (SD)	25.90 (5.05)	25.08 (4.38)	.997	.885	1.124	.962
Quality of psychological aspects, M (SD)	21.88 (4.43)	21.66 (3.44)	1.011	.879	1.162	.881
Quality of social relationships, M (SD)	11.13 (2.03)	10.36 (2.16)	1.179	.893	1.557	.246
Quality of environment, M (SD)	32.59 (5.75)	27.91 (5.91)	1.172	1.047	1.311	.006*
Symptomatic recovery, % (N)	51.9 (14)	44.2 (46)	1.024	.405	2.586	.960
General functional recovery, % (N)	53.4 (31)	40.7 (83)	1.433	.779	2.636	.247
Premorbid adjustment recovery, % (N)	52.5 (21)	43.4 (62)	1.228	.591	2.550	.582
Working recovery, % (N)	27.6 (16)	27.4 (52)	.745	.370	1.499	.409
Independent living recovery, % (N)	74.1 (43)	55.3 (105)	1.940	.987	3.813	.055
Insight recovery, % (N)	71.4 (40)	49.7 (88)	2.200	1.125	4.302	.021*

Note. N = total number. M = mean. SD = standard deviation. CI = confidence interval. LCI = Lower limit of the confidence interval; UCI = Upper limit of the confidence interval. All models were adjusted for gender and duration of untreated psychosis; OR_a = Adjusted odds ratio. Quantitative variables were treated as continuous variables. We used affective psychosis as the reference category of the dependent variable, all the results come from a bivariate analysis. *p<.05

4. Discussion

Our study aimed at exploring the clinical relevance of the dichotomy between affective and non-affective psychosis in a first episode psychosis sample. Based on our data, and despite many commonalities both at baseline and over the follow-up, in addition to gender and DUP previously reported (Conus et al., 2007; Kapila et al., 2019; Schothorst et al., 2006), these two sub-groups differed significantly regarding the course of positive, manic symptoms and insight, elements which might justify the development of distinct therapeutic approaches.

First, our results revealed important differences between affective and non-affective psychosis regarding the course of symptoms. Despite a similar trajectory, the level of positive psychotic symptoms remained higher in the non-affective sub-group. However, we did not find any differences between sub-groups regarding negative symptoms. These results are partially in line with previous studies comparing affective and non-affective groups, and reporting higher levels of both negative and positive symptoms at follow-up for the non-affective one (Henry et al., 2010; Kapila et al., 2019; Torrent et al., 2018). However, contrary to these previous studies, our study observed the course of psychotic symptoms over a three-year follow-up. Considering the crucial role of negative symptoms in long-term recovery (Austin et al., 2013), the absence of difference between affective and non-affective psychosis highlights the risk of poor long-term outcome in both disorders, confirming a challenging recovery previously reported in affective psychosis as well (Conus et al., 2010; Conus et al., 2006; Conus & McGorry, 2002). Our results suggest that positive symptoms remain the main distinctive symptomatic feature of non-affective psychosis. However, we did not investigate symptomatic trajectories within affective and non-affective psychosis to identify different patterns like previously found (Austin et al., 2015), it would thus be interesting to further explore the heterogeneity in the course of positive symptoms to develop targeted intervention. Moreover, considering mood symptoms, we found no difference in the course of depressive symptoms between affective and non-affective psychosis, and found that only the variability of manic symptoms was more important in affective psychosis. Previous literature on schizoaffective disorder reported similarities regarding treatment between schizophrenia and schizoaffective disorders,

especially depressed type (Keck, McElroy, & Strakowski, 1996), as well as similar outcome between schizoaffective disorder, major depression, and schizophrenia (Coryell, Grove, Keller, & Endicott, 1987). These results therefore suggest that the manic dimension may play an important role to differentiate affective from non-affective psychosis rather than the depressive one. Further investigation of such specificities within affective psychoses are however required to identify those not displaying the full blown mania syndrome considering that they are at risk of delayed identification (Arrasate et al., 2014; Conus, 2010) despite requiring specific treatment (Strakowski et al., 1998).

Second, we observed that patients with affective psychosis were more likely to develop insight over the treatment period than those with non-affective psychosis. Indeed, we found an early improvement of insight in the affective psychosis sub-group, which was significantly better after 6-month follow-up. This might be linked to the trait like condition of insight in non-affective psychosis contrasting with a state-dependent insight (Ghaemi & Rosenquist, 2004) associated with greater fluctuations of manic symptoms in affective psychosis, allowing for phases of full symptom recovery. Development of insight remains challenging in early psychosis, especially among patients with non-affective psychosis (Keshavan, Rabinowitz, DeSmedt, Harvey, & Schooler, 2004).

Third, regarding clinical data at entry, and as already reported previous publications (Conus et al., 2007; Kapila et al., 2019; Schothorst et al., 2006), gender and DUP differed significantly between affective and non-affective psychosis with a higher rate of women and a shorter DUP in the affective psychosis sub-group. However, contrary to these studies, we did not find any difference between groups regarding suicide attempts, past history of psychiatric disorder or substance use, premorbid functioning or adjustment, or psychotic and manic symptoms at baseline. Our results therefore suggest that premorbid and socio-demographic information may not provide clues to identify patients who will develop affective or non-affective psychosis contrary to previous findings regarding diagnosis identification (Kapila et al., 2019).

Fourth, while previous studies reported a better functioning and symptomatic recovery in affective than in non-affective psychosis (Kapila et al., 2019), our study did not reveal such differences. Nevertheless, this is in line with other studies suggesting that outcome in affective psychoses is not as good as

previously thought, especially regarding functioning (Conus et al., 2006). However, despite the absence of differences between sub-groups regarding clinical recovery, we found that the sub-group with affective psychosis had a better quality of environment at discharge. This may be linked to the fact that this subgroup had also a shorter DUP previously reported to be associated with a better quality of life (Marshall et al., 2005).

Finally, our findings suggest overall that affective and non-affective psychosis might benefit from specific intervention strategies like previously reported (Berk et al., 2017; Lambert et al., 2003). For example, a previous study on first-episode bipolar disorder reported that these patients benefit more of a mood stabilizer like lithium as maintenance treatment rather than an antipsychotic like quetiapine (Berk et al., 2017). In addition to treatment, Kessing et al. (2013) reported that patients in the early course of bipolar disorder may benefit from a specialized out-patients mood disorder clinic rather than standard care. However, further studies including schizoaffective disorder, major depression with psychotic features, and bipolar disorder patients are required to explore whether or not these patients with affective psychoses may benefit from a specific intervention targeting mood disorders.

Our results must be interpreted with some degree of caution due to various limitations. First, the six months interval between assessments may not enable to catch the complete feature of the course of symptoms through the early phase of illness. It would be interesting to study the course of mood symptoms with a greater sampling resolution and shorter time interval to better understand their temporal dynamic. Second, scores on the YMRS scale might be driven by symptoms such as delusions, insight and aggressive behaviour, rather than by specific manic symptoms, thus the similar levels of both groups on this scale must be considered with cautious. Third, we used the 2-month measures for the YMRS, MADRS, and PANSS as baseline measures which may not provide a very accurate baseline clinical picture. Indeed, during the first two months, treatment and case management follow-up are introduced providing the first steps for stabilization. Therefore, these measures do not reflect the acute baseline symptomatic picture of first episode patients, and may thus hide some clinical differences between affective and non-affective psychosis patients. However, the PANSS, YMRS, and MADRS measures were not available at baseline. Finally, differences between affective and non-affective

psychosis regarding the course of symptoms might be influenced be other variables that were not tested, like the type of medication. This would require further investigation.

5. Conclusion

Our study aimed to investigate the clinical relevance of a differentiation between affective and non-affective psychosis, and the results suggest that while this differentiation is challenging at baseline, it is nevertheless relevant, considering that these two groups display significant differences regarding their longitudinal trajectories and outcome. More studies are needed to explore the potential impact of a specification of intervention in both of these sub-groups.

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