Interactions between mood and paranoid symptoms affect suicidality in first-episode affective psychoses

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A B S T R A C T

Background: Suicide prevention is a major challenge in the treatment of first-episode affective psychoses. The literature reports that combinations of manic, depressive and paranoid symptoms, which may interact, are associated with an increased risk of suicide. The present study investigated whether interactions between manic, depressive and paranoid symptoms affected suicidality in first-episode affective psychoses.
Methods: We prospectively studied 380 first-episode psychosis patients enrolled in an early intervention programme and diagnosed with affective or non-affective psychoses. We compared intensity and presence of suicidal thoughts and occurrence of suicide attempts over a three-year follow-up period and investigated the impact of interactions between manic, depressive and paranoid symptoms on level of suicidality.
Results: At 12 months follow-up, we observed a higher level of suicidal thoughts and higher occurrence of suicide attempts among the affective psychoses patients compared to non-affective psychoses patients. Combined presence of either depressive and paranoid symptoms, or manic and paranoid symptoms, was significantly associated with increased suicidal thoughts. However, the combination of depressive and manic symptoms showed a significant negative association with suicidal thoughts.
Conclusions: This study suggests that paranoid symptoms combined with either manic or depressive symptoms are associated with an increased risk of suicide in first-episode affective psychoses. Detailed assessment of these dimensions is therefore warranted in first-episode affective patients and integrated treatment should be adapted to increased suicidal risk, even if patients do not display full-blown depressive or manic syndromes.

1. Introduction

Suicidality is a major contributor to premature mortality in first-episode psychosis (Pompili et al., 2011; Robinson et al., 2009; Robinson et al., 2010). Vulnerability to suicidal behavior may be particularly significant among patients combining symptoms of mood and psychotic disorders (Bostwick and Pankratz, 2000). Suicidality is thus a primary concern for those with early affective psychoses (Miller and Black, 2020), including major depressive and bipolar disorder with psychotic features, and for patients with schizoaffective disorder, who show high rates of suicidal thoughts or behaviours (Berk et al., 2007; Bostwick and Pankratz, 2000; Gaudiano et al., 2008; Miller and Black, 2020; Radomsky et al., 1999).

Psychopathological features associated with suicidality have been investigated previously. A study on 4502 inpatients reported that both bipolar and unipolar depressed patients faced a high risk of suicide, especially those with a depressive and paranoid-hallucinatory syndrome. Another prospective study (Axelsson and Lagerkvist-Briggs, 1992) found that depressive mood, elated mood and paranoid ideas were all significantly correlated with suicide. In line with that, another study (Cassidy et al. (2001)) identified a subtype of mania, with co-occurring depressive and paranoid symptoms, which was associated with more suicidal ideation than pure types of mania (without depressive symptoms). One review (Miller and Black, 2020) concluded that depressed or mixed subtypes of mania, but not pure mania were associated with suicide. These findings suggest, therefore, that the co-occurrence of manic, depressive and paranoid symptoms was probably associated with increased risks of suicide. This is particularly concerning

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considering that persecutory delusion is very common among patients suffering from a manic-depressive illness with psychotic features (Dunayevich and Keck, 2000). Indeed, a study in a cohort of 108 patients with first-episode of psychotic mania showed that 72.5 % of them displayed persecutory delusions, which was true in bipolar patients where the rate was 69 %, as well as in schizoaffective patients where the rate was 85.7 % (Conus et al., 2004).

Furthermore, previous studies have reported associations between mood dysregulation and paranoid ideation (Fowler et al., 2012; Freeman et al., 2002; Lake, 2008) and have suggested a possible interplay between manic, depressive and paranoid elements (Akiskal et al., 2003; Conus et al., 2008). In sum, relationships between suicidality and mood and paranoid symptoms have been previously reported, as well as possible interactions between manic, depressive and paranoid symptoms. However, to the best of our knowledge, the nature of such interactions in suicidality has never been investigated. The present study's aims were, therefore, to explore (1) the courses of suicidality in first-episode affective and non-affective psychoses, and (2) the interactions between the depressive, manic and paranoid symptoms associated with increased suicidality in affective psychoses. Given that paranoid symptoms combined with either manic or depressive symptoms might be associated with increased suicidality, we hypothesised that patients suffering from affective psychoses could be differentially affected by those variables. Exploring these interactions would help provide a better understanding of the underlying psychopathological mechanisms of suicidality and, therefore, could aid suicide prevention.

2. Method

2.1. Sample and procedure

This is a prospective study in a cohort of first-episode psychosis patients treated at the Treatment and Early Intervention in Psychosis Programme (TIPP) in Lausanne University Hospital's Department of Psychiatry (Baumann et al., 2013; Conus and Bonsack, 2004). The sample and procedure of data collection have already been described in details in a previous study (Ramain et al., 2021).

2.2. Diagnostic assessment

The diagnoses (DSM-IV criteria) resulted from an expert consensus after discussions held at 18 and 36 months, using information from patients' medical records or hospitalisation reports provided by their treating psychiatrists and their TIPP-assigned psychiatrists and case managers. In this study, the latest consensus diagnosis available was used. Patients included in the affective psychoses group were diagnosed with major depressive disorder or bipolar disorder with psychotic features or with schizoaffective disorders; those in the non-affective psychoses group were diagnosed with schizophrenia or other schizophreniform disorders. Patients diagnosed with unspecified psychosis were excluded as this diagnosis was considered unstable (Cawkwell et al., 2020; Taş et al., 2019), and the status between affective and non-affective psychoses was unclear.

2.3. Sociodemographic characteristics

Sociodemographic variables were reported by case managers. We divided the socioeconomic status (SES) into low, intermediate and high categories (Chandola and Jenkinson, 2000). Patients living without supervision in independent households were referred as *independent living*. Their employment situations were subdivided into active employee (partial/full-time employment), student/apprentice or other. According to the CAARMS criteria (Yung et al., 2005), we defined duration of untreated psychosis (DUP) as the time elapsed between the onset of psychosis and admission into the TIPP.

2.4. Clinical presentation at programme initiation

We compared the symptomatology of the affective and non-affective psychoses groups at programme initiation. The first available measures of symptomatology were at the two-month follow-up, and these measures were used to provide a picture of the sample's clinical presentation early on in the programme. We assessed the severity of depressive symptoms using the Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery and Åsberg, 1979) and manic symptoms using the Young Mania Rating Scale (YMRS; Young et al., 1978). Positive and negative psychotic symptoms, together with general symptomatology, were measured using the Positive and Negative Psychotic Syndrome Scale (PANSS; Kay et al., 1987). Case managers rated insight as being absent, partial, or full with regards to awareness of illness and the necessity of treatment.

2.5. Suicidality

We used two different measures of suicidality: suicidal thoughts and suicide attempts reported at 2, 6, 12, 18, 24, 30 and 36 months. We used the suicidal thought item from the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1988) and considered occurrences of suicide attempts or their absence, as reported by case managers at follow-up assessments. We also examined occurrences of past suicide attempts.

2.6. Severity of paranoid, depressive and manic symptoms

Assessments of paranoid, depressive and manic symptoms were done at 2, 6, 12, 18, 24, 30 and 36 months of follow-up. The MADRS was used to assess the severity of depressive symptoms, the YMRS for manic symptoms, and the suspiciousness/persecution item of the PANSS for paranoid symptoms.

2.7. Statistical analysis

We began by conducting a logistic regression analysis of the main sociodemographic measurements (i.e. age, sex, SES, DUP, age at onset) to explore statistical differences between affective and non-affective psychoses at programme initiation. Because affective and non-affective psychoses differed according to sex, DUP and age at onset, these three variables were included in the following models. For this group comparison, the affective psychoses group (Yes/No) was introduced as the dependent variable and the symptomatology scores at the two-month follow-up (MADRS, YMRS, PANSS and insight) were added as predictors (one at a time for each model).

We used a mixed-effects model with repeated measures of analysis of variance (Mixed-Models-for-Repeated-Measures, MMRM) to evaluate the differences in suicidal thoughts between groups over time. We used time as a "within-group" factor and group as a "between-groups" factor. The main effects for the affective psychoses group and time can be examined from the model, as well as their interaction. We used the Akaike information criterion coefficient to select the optimal within-subject covariance matrix in each MMRM. We also compared occurrences of suicide attempts and adherence to treatment or medication (lithium, amisulpride) during follow-up in both groups using chi-square tests.

Because the data indicated a rise of suicidality at the 12-month follow-up, we tested the interaction effects of mood and paranoid symptoms on suicidal thoughts at this time point using a regression analysis for each group. To do this, the coefficients of the three two-way interactions and the three-way interaction were estimated. We centred every independent variable (manic, depressive and paranoid symptom scores) and controlled for insight by considering its association with suicidal behavior (Crumlish et al., 2005; Kim et al., 2003; Schwartz and Smith, 2004). The analyses were performed using the IBM SPSS software (version 26) and the Mplus software (version 7.4).

3. Results

3.1. Sociodemographic characteristics

We reported the sociodemographic characteristics of the affective and non-affective psychoses groups in Table 1.

3.2. Clinical presentation at programme initiation

We found no significant differences between the affective and non-affective psychoses groups regarding manic, depressive, psychotic and general symptoms two months after programme initiation (Table 2). The groups also showed no difference regarding insight at baseline.

3.3. Suicidality in affective and non-affective psychoses

Regarding past suicide attempts, rates did not significantly differ (χ^2 (1) = 0.396; p = .568) between the affective (16.2 %; n = 12) and the non-affective psychosis group (13.3 %, n = 34). During the three-year follow-up, the total rates of patients who committed at least one suicide attempts did not differ significantly (χ^2 (1) = 2.408; p = .188) between the affective (10.7 %, n = 8) and the non-affective psychosis group (5.6 %, n = 15). In the affective psychosis group, longitudinal analysis revealed a significant decrease in suicidal thoughts between the 2- and 6-month follow-ups (mean difference = −0.516; df = 224.934; p = .017) and a significant increase in suicidal thoughts between the 6- and 12-month follow-ups (mean difference = 0.487; df = 234.975; p = .030; Fig. 1). In the non-affective psychosis group, suicidal thoughts

significantly decreased during follow-up (F (6, 197.248) = 2.161; p = .048; Fig. 1). We found a significant difference between the groups when looking exclusively at suicide attempts after 12 months, with significantly more suicide attempts in the affective psychoses group (χ^2 (1) = 7.174; p = .02). We verified whether there were any relationships with adherence to treatment or medication but found no significant differences between groups across the 36 months of follow-up.

3.4. Effects of interactions between paranoid, manic and depressive symptoms on suicidal thoughts in affective and non-affective psychoses groups at 12-months follow-up

The coefficient of the three-way interaction between paranoid, manic and depressive symptoms on suicidal thoughts was not significant in the affective psychoses group (β = −0.123, p = .339). However, the interaction between paranoid and depressive symptoms on suicidal thoughts was significant (β = 0.382, p = .001; Fig. 2A), as well as was the interaction between paranoid and manic symptoms (β = 0.797, p < .001; Fig. 2B), such that more severe depressive and paranoid symptoms, or more severe manic and paranoid symptoms, were associated with more suicidal thoughts. The coefficient of the two-way interaction between manic and depressive symptoms on suicidal thoughts was also significant (β = −0.772, p < .001; Fig. 2C); it was more important than the sum of the individual effects of manic symptoms (β = 0.112, p = .340) and depressive symptoms (β = 0.435, p < .001), indicating that the combination of more severe manic and depressive symptoms were associated with fewer suicidal thoughts.

In the non-affective psychoses group, the interaction between depressive and paranoid symptoms was the only one significantly associated with and increased level of suicidal thoughts (β = 0.232, p = .039).

4. Discussion

This study aimed first to explore the evolution of suicidality and the occurrence of suicide attempts in first-episode affective psychoses, and second whether interactions between depressive, manic and paranoid symptoms were associated with an increased suicidality, and to which extent such patterns were specific to the affective psychosis group. Our results show an increase in suicidal thoughts in affective psychoses patients at the 12-month follow-up,—something which did not occur in non-affective psychoses patients. This was confirmed by more suicide attempts among affective psychoses group members at 12 months. The two groups did not differ concerning past suicide attempts though. Furthermore, regression analyses revealed that paranoid symptoms were probably a key element which significantly raised suicide risk among affective psychosis patients presenting with mood symptoms. Indeed, combinations of either more severe depressive and paranoid symptoms or more severe manic and paranoid symptoms, were significantly associated with increased suicidal thoughts in affective psychoses patients. However, as highlighted by the negative two-way interaction, suicide risk was significantly reduced by the simultaneous presence of more severe manic and depressive symptoms.

Our results suggest that paranoid symptoms increase suicidality when they co-occur with mood symptoms among patients with affective psychoses. Although mood-incongruent psychotic symptoms were previously reported as having no effect on outcomes at 12 months among first-episode manic patients (Conus et al., 2004), their presence may worsen suicidality, especially when co-occurring with manic symptoms. Although manic symptomatology in itself may have no effect on suicidality (Persons et al., 2018), its impulsivity component, when co-occurring with paranoid ideation, seems to lead to an increase risk of suicide (Dutta et al., 2011). In this regard, clinicians should consider paranoid symptoms as a red flag suggesting a significantly increased suicide risk when co-occurring with mood symptoms in affective psychosis patients. More studies are needed to determine whether other

Table 1
Sociodemographic characteristics of the affective and non-affective psychosis groups.

	Total	Affective psychosis	Non-affective psychosis
	N = 343	N = 75 (21.90 %)	N = 268 (78.10 %)
Gender, male % (N)	65.0 (223)	52.0 (39)	68.7 (184)
Age in year, M (SD)	24.50 (4.61)	25.17 (4.90)	24.31 (4.52)
Socio-economical level, % (N)			
Low	38.2 (131)	38.7 (29)	38.1 (102)
Intermediate	43.1 (148)	42.7 (32)	43.3 (116)
High	18.7 (64)	18.7 (14)	18.7 (50)
Living situation, % (N)			
Independent	68.1 (226)	67.1 (49)	68.3 (177)
Others	31.9 (106)	32.9 (24)	31.7 (82)
Employment situation, % (N)			
Active	14.2 (48)	18.1 (13)	13.2 (35)
Student/Traineeship	18.0 (61)	26.4 (19)	15.8 (42)
Others	67.8 (229)	55.6 (40)	71.1 (189)
Education in year, M (SD)	10.10 (2.75)	10.56 (2.60)	9.98 (2.78)
Marital status, % (N)			
Single	84.6 (285)	79.7 (59)	85.9 (226)
Married	8.6 (29)	12.2 (9)	7.6 (20)
Divorced	3.3 (11)	5.4 (4)	2.7 (7)
Cohabitation	3.6 (12)	2.7 (2)	3.8 (10)
Diagnosis % (N)			
Schizophrenia	64.4 (221)		82.5 (221)
Schizophreniform disorder	13.7 (47)		17.5 (47)
Schizoaffective disorder	9.9 (34)	45.3 (34)	
Major depression with psychotic features	4.7 (16)	21.3 (16)	
Bipolar disorder	7.3 (25)	33.3 (25)	
Age of onset, M (SD)	23.10 (4.97)	22.80 (4.93)	24.17 (5.03)
Duration of untreated psychosis (days), Mdn (IQR)	97.00 (479.00)	49.00 (174.00)	116.00 (577.50)

Note. M = mean. SD = standard deviation. Mdn = median. IQR = interquartile range. [a] physical or sexual abuse.

Table 2

Clinical presentation of affective and non-affective psychosis at the beginning of the programme.

	Total	Affective psychosis	Non-affective psychosis	OR$_a$	95 % CI of OR$_a$		p-value
	N = 343	N = 75 (21.90 %)	N = 268 (78.10 %)		LCI	UCI	
YMRS at the beginning, M (SD)	6.66 (5.94)	6.03 (5.40)	6.86 (6.11)	0.972	0.902	1.048	0.463
MADRS at the beginning, M (SD)	15.67 (9.80)	17.47 (11.40)	15.09 (9.23)	1.030	0.986	1.075	0.184
PANSS at the beginning, M (SD)							
Positive	13.64 (4.95)	12.77 (4.24)	13.91 (5.14)	0.959	0.877	1.048	0.357
Negative	16.17 (6.06)	15.23 (5.27)	16.47 (6.28)	0.972	0.904	1.044	0.433
General	34.36 (8.31)	34.39 (6.86)	34.35 (8.74)	1.000	0.951	1.050	0.991
Insight at baseline, % (N)				0.964	0.670	1.388	0.843
Full	21.7 (72)	23.6 (17)	21.2 (55)				
Partial	45.5 (151)	41.7 (30)	46.5 (121)				
Null	32.8 (109)	34.7 (25)	32.3 (84)				

Note. M = mean. SD = standard deviation. CI = confidence interval. YMRS, Young Mania Rating Scale; MADRS, Montgomery-Asberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale. OR$_a$ = Adjusted odds ratio. We adjusted all models for gender, duration of untreated psychosis, and age of onset. We treated quantitative variables as continuous variables. The reference category of the dependent variable was affective psychosis.
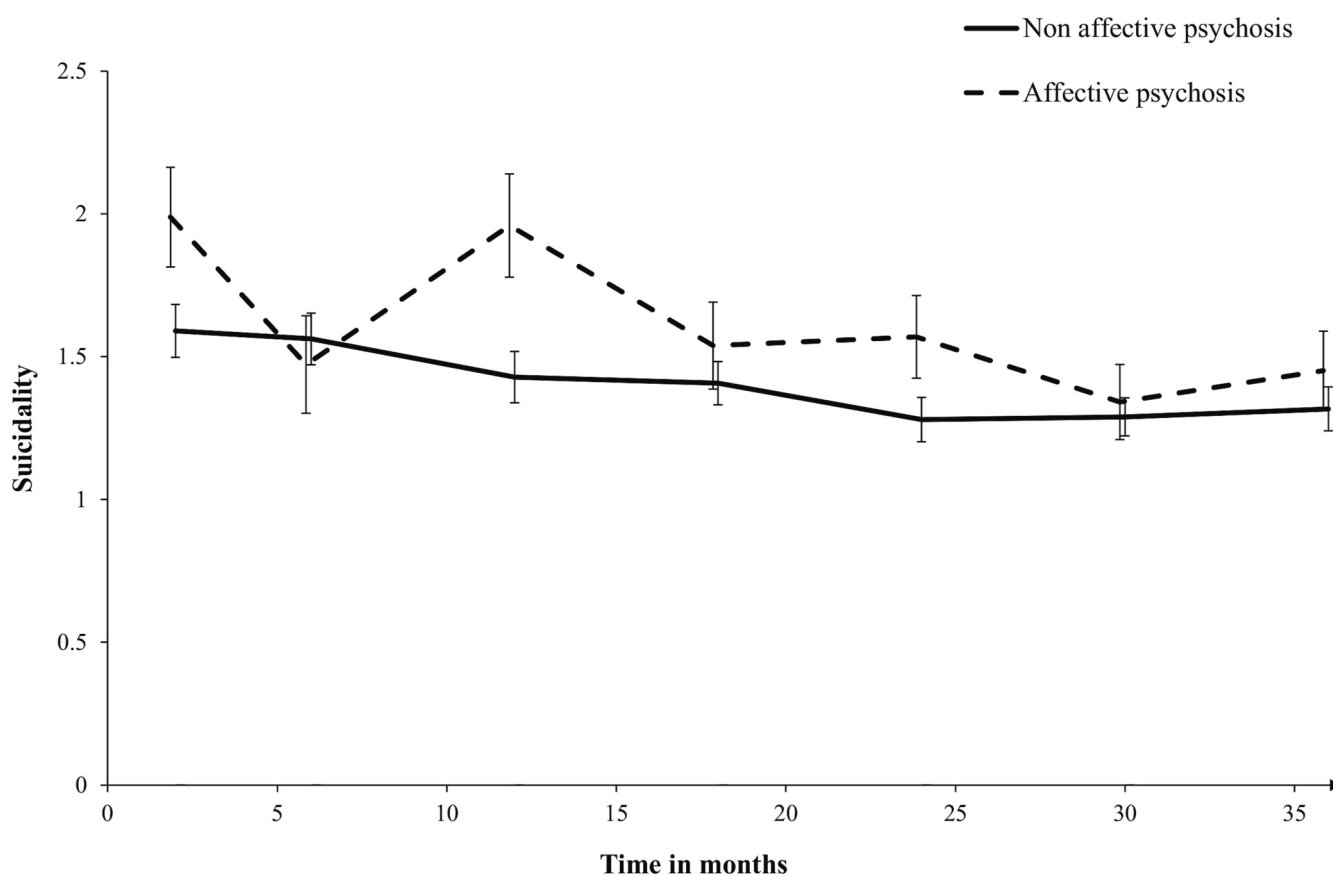
Fig. 1. The course of suicidal thoughts over 3 years follow-up in affective and non-affective psychosis.

psychotic dimensions might play a similar role when interacting with mood symptoms.

Our findings revealed that the interaction between depressive and paranoid symptoms as well led to an increase in suicidal thoughts. This is in line with a large representative study of bipolar and unipolar depressed patients, where risk of suicidal behavior was especially high among those where depressive and paranoid-hallucinatory syndrome coexisted (Bottlender et al., 2000). In this study, this interaction was also significant in non-affective psychosis patients, suggesting that the co-occurrence of depressive and paranoid symptoms could as well represent a red flag for clinicians when assessing suicide risk, and thus independently of the affective component of the psychoses Taken together, these results strengthened our hypothesis that paranoid symptoms probably play a crucial role in suicidality.

Another key finding in our study was the limitations to suicidality appearing with the presence of both depressive and manic symptoms. This was surprising, considering that mixed subtypes are known to face higher risk of suicide (Miller and Black, 2020), especially among young patients (Lage et al., 2019; Saxena et al., 2020). A previous long-term prospective study reported that patients with bipolar or unipolar disorders with a history of mixed states were more likely to attempt suicide (Persons et al., 2018). Furthermore, those authors also reported that although the manic component, contrary to the depressed one, had no significant effect on suicidal behavior, patients with a bipolar or unipolar disorder and a history of mixed states spent more time depressed than those without a history of mixed states (Persons et al., 2018). Consequently, our results suggest that suicidal thoughts are limited during mixed states in the early course of a psychotic illness, with manic
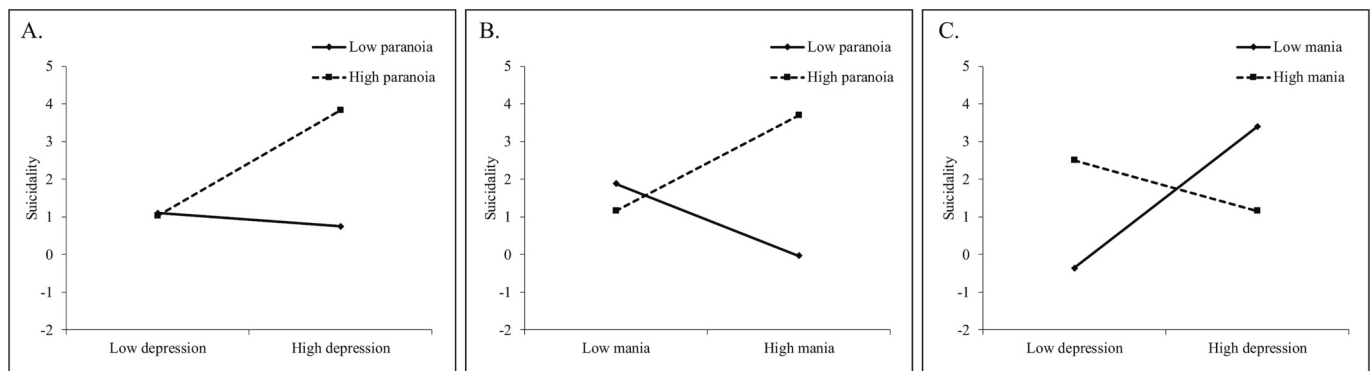
Fig. 2. Interaction effects between depression and paranoia (A), mania and paranoia (B), depression and mania (C) on suicidal thoughts in affective psychosis at 12 months follow-up.

symptoms playing a defensive role against the suicidal thoughts associated with depressive symptoms. Nevertheless, although suicidal thoughts might be limited during mixed states in the short term, mixed states increase the risk of chronicity(Persons et al., 2018; Schürhoff et al., 2000; Swann et al., 2001; Swann et al., 2013) and are associated with more time spent depressed, and therefore with a higher risk of suicide in the long term (Persons et al., 2018). Thus, the long-term counter effects of the manic dimension in mixed states should be considered attentively in any early intervention to prevent suicide. Our results may also be explained by the fact that we report on depressive and manic dimensions based on MADRS and YMRS scores, and not on threshold diagnosis of depression and mania.

Finally, higher suicidality at the 12-month follow-up was observed in affective but not in non-affective psychoses patients, regardless of the effects of medication or adherence to treatment. This suggests that patients with first-episode affective psychoses may be particularly vulnerable to suicide at the end of their first year of treatment, which might be linked to their improvement in insight after 6 months of follow-up (Ramain et al., 2021)—the so-called "insight paradox" (Murri et al., 2015). Systematic and regular assessments of suicide risk is therefore crucial during the first year of any early intervention programme, as well as a detailed psychopathological assessment of mood and paranoid symptoms. Indeed, as mentioned above, the correlations we report are based on scores on depression and mania scales rather than on full-blown depressive or manic syndromes, suggesting that subthreshold depressive and manic elements should also be taken into account when assessing suicidal risk in such patients.

Some of our findings must be interpreted with caution and considering the study's limitations. First, the affective psychoses group was relatively small and included a majority of patients diagnosed with a schizoaffective disorder. Our results would thus require replication in a larger sample of first-episode affective psychosis patients and with higher numbers in bipolar and depressive patients. Second, the level and intensity of care in our three-year programme is need-adaptive, with the probability that care was intensified when necessary and included systematic intervention in cases involving a suicide risk, which may influence results and limits generalizability of our results to programmes where such adaptation is not possible.

5. Conclusions

The present study aimed to explore the course of suicidality among patients experiencing first-episode affective psychoses, as well as the link between suicidality and the interactions between mood and psychotic paranoid symptoms. Our findings suggest that patients experiencing first-episode affective psychoses may be particularly at risk of suicide at the end of their first year of treatment and that patients presenting with paranoid symptoms, particularly when combined with

either manic or depressive symptoms, have an increased risk of suicide. Clinicians should therefore conduct regular and detailed assessment of symptoms and should consider them as red flag, even when depression or mania threshold are not reached, and adapt treatment on this basis.

CRediT authorship contribution statement

Julie Ramain (JR), Philippe Conus (PC), Philippe Golay (PG). PG & PC designed this research. JR acquired the data. PG, JR, and PC analysed and interpreted the data. PG and JR drafted the first version of the manuscript. PG & PC critically revised the manuscript for important intellectual content.

Declaration of competing interest

None.

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