A Study of the Real-World Effectiveness of Group Psychoeducation for Bipolar Disorders: Is Change in Illness Perception a Key Mediator of Benefit?

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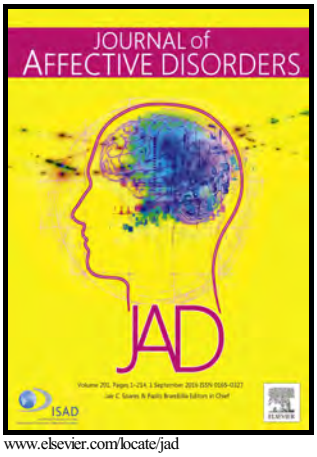

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A study of the real-world effectiveness of group psychoeducation for bipolar disorders: is change in illness perception a key mediator of benefit?

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ABSTRACT (n=250)

Background: Findings from efficacy trials of group psychoeducation (PE) for bipolar disorders (BD) led to its inclusion in evidence-based guidelines as a first-line mandatory treatment. However, pragmatic trials and observational studies are needed to determine its real-world effectiveness, impact on outcomes deemed important to patients and to clarify potential mediators of any benefits.

Methods: Individuals with BD were offered the opportunity to participate in 20 hours of PE and asked to complete pre- and post-intervention ratings of symptoms, knowledge about BD, medication adherence, and illness perception. *A priori*, two key patient outcomes were identified (social functioning and self-esteem); sample attrition due to dropout or relapse was recorded.

Results: Of 156 individuals who completed the pre-PE assessments, 103 completed the program and post-PE assessments. Only 4 of 53 dropouts were associated with BD relapse. Post-intervention, the PE completers demonstrated a statistically significant improvement in social functioning ($p=0.003$, Effect Size (ES)=0.26) and a trend towards improved self-esteem (ES=0.14). Whilst there were significant changes in medication adherence ($p=0.002$, ES=0.28), knowledge of BD ($p<0.001$, ES=1.20), and illness perception ($p<0.001$, ES=-0.37), mediational analysis demonstrated that only change in illness perception was associated to change in functioning ($p=0.03$) with no contribution from changes in knowledge of BD or medication adherence.

Conclusions: In real-world settings, over 60% individuals completed 10-session course of PE. After controlling for demography and baseline clinical state, change in illness perception, rather than change in knowledge or medication adherence, emerged as a potential mediator of some benefits of PE.

Key words: bipolar disorders, psychoeducation, effectiveness, illness perception, mediators, functioning.

INTRODUCTION

Bipolar disorders (BD) affect 1-4% of the population, causing significant mortality, morbidity and psychosocial adversity (Goodwin F, 2009.; Murray and Lopez, 2013). It is acknowledged that optimal treatment of BD cannot rely on pharmacotherapy alone, and clinical practice guidelines recommend the use of psychological interventions, such as psychoeducation (PE) as a first line maintenance treatment (Yatham et al., 2013). These recommendations arose because randomized controlled trials (RCTs) repeatedly demonstrated the efficacy of group PE in preventing BD relapses in individuals who commenced therapy during euthymia.

Whilst many elements of efficacy RCTs help to minimize confounding and bias (e.g. recruitment of homogeneous samples of euthymic cases) and maximize opportunities to detect treatment effects (Carroll and Rounsaville, 2003), the consequences can be a loss of external validity and generalizability (Scott, 2008). For example, (Hoertel et al., 2013) demonstrated that more than 50% individuals with BD would be excluded from most efficacy RCTs (58-64% for depression; 56% for mania), and that excluded cases were those that were least likely to respond to the experimental treatment. Also, the endpoints and outcome measures employed in efficacy studies primarily focus on targets that are of most concern to health care providers (e.g. relapses, admissions, cost) (Camacho et al., 2017), rather than benefits that are the most meaningful to patients (e.g. concerns about functioning and self-esteem, etc.) (Jonas et al., 2012). Lastly, knowledge of the clinical predictors or moderators of response to PE and other therapies (such as prior number of BD episodes) does not always shed light on the mediators of any therapeutic effects (in contrast to studies of putative mechanisms of action of medications) (Calabrese and Kemp, 2008). Given these issues, it is important to continue to evaluate interventions after they are transferred to general psychiatry settings to understand any efficacy-effectiveness gaps (Blanco et al., 2013).

Recent studies of PE have begun to address the above concerns, demonstrating practical barriers to delivering group PE in day to day practice (Biseul et al., 2016; Coulthard et al., 2013), and/or patient preferences for shorter duration of therapy (Kallestad et al., 2016). Furthermore, PE may be less effective when offered to heterogenous BD populations with complex or unstable (non-euthymic) presentations, and/or if delivered by less able therapists (Biseul et al., 2016; Bond and Anderson, 2015; Kallestad et al., 2016; Morriss et al., 2016). These findings do not detract from the importance of offering group PE in routine clinical settings, but attest to the need for comparative effectiveness research (CER) (National Research Council, 2009), which encompasses a range of methodologies including prospective observational monitoring of patient-related outcomes and use of self-ratings in broader clinical samples than recruited to RCTs (Berger et al., 2009; Marko and Weil, 2010).

Although these CER approaches are gaining acceptance in psychiatry (Friedman et al., 2014), their role with therapies is underexplored compared to medications (Lambert, 2017; Porzsolt et al., 2015). As such, we report a feasibility, or 'proof of principle' study that assessed individuals with BD from the point of acceptance of an invitation to participate in PE through to dropout from or completion of a group programme delivered in a day-to-day clinical setting and that included patient-focused outcomes. We specifically explored:

1. Adherence / Attrition: How many cases that completed the pre-PE assessments and commenced the course of therapy also completed the programme and the post-PE assessments? What are the baseline characteristics associated with dropout and the commonest reasons for sample attrition?
2. Therapy Outcomes: How many relapses are observed during the intervention period? Are there any significant pre- to post-PE changes in mood and anxiety symptoms or in the two patient-focused outcomes, namely social functioning and self-esteem?
3. Mediators: Is it possible to identify any full or partial mediators of therapeutic effects of PE on the patient-orientated outcome measures? The mediators were selected after a review of the empirical literature published during the last decade. This identified that knowledge about BD, medication adherence and illness perception have all been specifically targeted in PE programs and have been identified or proposed as putative mediators of the effects of PE (see appendix 1). For example, it was noted that PE could enhance medication adherence (Gonzalez-Pinto et al., 2004; Miklowitz and Scott, 2009; Vieta, 2005), but also that PE can also be beneficial in individuals who show high levels of medication adherence (Colom et al., 2003b), leading to investigations of the potential importance of health beliefs and illness-awareness (Colom and Lam, 2005).

METHODS

As group PE and monitoring of outcome are part of routine clinical practice in the service where the study was undertaken, the local ethical committee gave approval for this project as a 'treatment as usual' study (for additional details about this classification see (Biseul et al., 2016)). Individuals offered to option of participation in group PE were first provided with an information sheet about the programme, after which they had to demonstrate their interest in PE by 'opting-in' (i.e. initiating a preliminary appointment to discuss joining a PE group). Individuals identified as eligible for PE were then given a letter explaining that, unless they refused to give consent, their de-identified assessment data would be included in an evaluation of the benefits of PE. The ethical committee does not permit data collection about, nor any contact with: (i) clinic attendees with BD who were not referred to the group PE programme, or (ii) individuals who did not 'opt-in' to a discussion about PE participation.

Participants

a) Sample Recruitment:

Local psychiatrists working in the public and private sector in the catchment area surrounding the Creteil district of Paris were invited to refer individuals with a primary diagnosis of BD for potential participation in PE. The period of data collection was 2008 to 2015. During the same period, we received around 450 letters from psychiatrist who would like to refer their patients to the psychoeducation programme. All of these referred patients have received a letter for an invitation to contact us for their participation. Of these, only 156 effectively came to participate, leading an estimate of around 35%. For the 450 potential participants, ethical constraints precluded retrieval of further information.

b) Eligibility:

The only exclusion criteria for group PE were: (i) deafness or other impairments to communication (e.g. difficulties in comprehending the French language); and (ii) a current diagnosis of social phobia, severe alcohol or substance misuse, severe antisocial or borderline personality disorder, and/or impaired intellectual capacity. Participation in PE was delayed for about three months (to allow a period of stabilization) for individuals with a Young Mania Rating Scale score >=8 (YMRS) (Young et al., 1978), and/or a Montgomery Asberg Depressions Scale (MADRS) score >=15 (Montgomery and Åsberg, 1979), and/or if the individual had experienced a recent acute BD episode. Whilst all PE participants were encouraged to continue with ongoing prescribed interventions (e.g. pharmacotherapy and social support, etc.), failure to do so was not an exclusion criterion.

Psycho-education intervention

The PE intervention closely followed the programme described in the manual by Colom and Vieta (Colom et al., 2006), but was modified to allow completion over 10 sessions (of 120 min each) which were delivered over three months and supplemented by between-session learning exercises and homework assignments (additional details in Appendix 1). Each PE group comprised of 7-11 individuals with BD and sessions were conducted by a psychologist and a psychiatrist (with >5 years of clinical experience of working with BD, and specific training in groups and CBT).

Assessments

Participants were asked to attend three individual meetings. During two pre-intervention meetings, individuals received information about the aims of the PE group, eligibility for participation was confirmed, and observer and self-rated assessments were completed (within three weeks of starting therapy). The post-intervention meeting incorporated repeated assessments and feedback about the

group (completed within three weeks of finishing therapy).

Data were collected on the following:

a) Baseline only : Socio-demographics and basic clinical characteristics e.g. subtype of BD (according to DSM-IV) and prior history of illness (including e.g. suicide attempts and hospitalizations).

b) Pre- and post-PE symptom ratings: current mood symptoms using the MADRS and YMRS (Montgomery and Åsberg, 1979; Young et al., 1978); and state and trait anxiety measured using the State Trait Anxiety Inventory (STAI-A and STAI-B; (Spielberger, 1983)).

c) Attrition rate: number of and reasons for PE non-completion (dropout; BD relapse; failure to complete post-PE ratings) were recorded. Individuals were withdrawn from the PE programme if they experienced a manic or depressive relapse, and/or they missed >=2 sessions (as non-attendance of >=20% of the programme led to noticeable problems in maintaining group involvement or completing skills development tasks).

d) Key outcomes: we examined any changes between pre- and post-PE levels of self-esteem (Coopersmith, 1967) and social functioning (Zanello et al., 2006). The adult version of the Coopersmith self-esteem inventory is widely used and comprises of 58 items (rated by the individual as 'like me' or 'not like me'), with scores <33 indicative of low self-esteem. The Questionnaire de Fonctionnement Social (QFS) (Zanello et al., 2006) is a self-report instrument that assesses the frequency of (8 items) and satisfaction with (8 items) performance on different social activities during the preceding two weeks. Scores range from 16-80, with higher scores indicative of better functioning.

e) Putative mediators of PE effectiveness: changes in medication adherence, knowledge about BD and cognitive and emotional representations of illness were selected a priori for mediational analysis. Medication adherence was assessed using the Medication Adherence Rating Scale (MARS; (Thompson et al., 2000); scores range from 0 to 10 with lower scores indicating higher levels of medication adherence. The 'Knowledge about BD' questionnaire consisted of 20 true/false questions about important aspects of BD (e.g. questions about prevalence, symptoms, likelihood of relapse, genetic predisposition etc.), and a higher score indicates greater knowledge about BD. The questionnaire was constructed by the authors to reflect similar English language instruments in the literature, but has not yet been validated.

   Cognitive and emotional representations of illness were measured using the revised version of the Brief Illness Perception Questionnaire (IPQ) (Broadbent et al., 2006). Each item on the questionnaire is rated on a 0-10 scale to determine the individual's perceptions about the causes and controllability of BD. The version used in this study comprised of nine items, as an additional self-report item (asking individuals to rate on a 0-10 scale 'How much do you agree with your diagnosis of bipolar disorder?') was used to replace an open-ended question that had previously

proved difficult to score reliably (Scott, 2002). We used the global score (ranging from 0 to 90) in the analyses, with a higher value indicating more negative illness perceptions (with less adaptive coping and/or impaired illness awareness). In studies of BD or other persistent mental or physical illnesses, mean IPQ scores on the 8-item questionnaire are about 49-52 (Broadbent et al., 2006).

Statistical analyses

Data analyses were performed using SPSS version 23.

Descriptive statistics were used to identify the proportion of non-completers and examine any demographic and clinical differences between the completers and non-completers using chi-squared or Fisher's exact tests, and Wilcoxon rank sum or t-tests as appropriate.

In the completer only sample, we explored the statistical significance of any pre- and post-PE changes in mood and anxiety symptoms, and in key outcomes (social functioning and self-esteem) using paired t-tests. For the putative mediators of outcomes (medication adherence, knowledge about BD and illness perception), we report the significance of pre- to post-PE changes, the magnitude of any change using effect sizes (ES) (Cohen, 1988), and Spearman's correlations for associations between these three variables and any statistically significant outcome measures. Finally, we used two different ways to explore potential mediation. The first model was a backward linear regression designed in four blocks. Analyses explored the associations between QFS after and QFS before, changes in knowledge, illness perception and adherence (block 1), then adjusted for baseline values of knowledge, illness perception and adherence (block 2), then adjusted for baseline values of depressive and anxiety symptoms (block 3), finally adjusted for age and gender (block 4). The second model was based on the Preacher and Hayes' model testing for mediation effects. We used the PROCESS macro for SPSS (http://afhayes.com/spss-sas-and-mplus-macros-and-code.html) to perform the mediation analysis (Hayes, 2012). Mediation implies a situation where the effect of the independent variable on the dependent variable can best be explained using one or several mediator variables that are caused by the independent variable and are themselves a cause for the dependent variable. In brief, using a series of regression analyses, the model explores whether X is causing Y directly or whether X is causing the mediator M, and M is in turn causing Y. The causal relationship between X and Y in this case is said to be indirect. The model was as follows: X was the change of illness perception, and Y was the change in functioning. Since PROCESS allows including several mediators, we included changes in knowledge about BD and in adherence as potential mediators. The relationships between the independent variable, the mediators, and the dependent variables are depicted in the form of a path diagram/model. For each path, the regression coefficients (betas) indicating the direction and magnitude of the effect of one variable on the other are shown.

Bootstrapping, a nonparametric resampling procedure that does not impose the assumption of normality of the sampling distribution, was conducted. Mediation analyses were tested using the bootstrapping method with bias-corrected confidence estimates. In the present study, the 95% confidence interval of the direct and indirect effects was obtained with 10 000 bootstrap samples. Indirect effects are significant if confidence intervals do not contain a zero value.
Given the nature of the study, it is important to correct for multiple testing. We used the FDR (False Discovery Rate) approach advocated by Benjamini and Hochberg (Benjamini and Hochberg, 1995) , the significant threshold for p values was identified as 0,009 (Simes, 1986). Mediation analyses were not included in this calculation since we considered these as post-hoc analyses.

RESULTS

Participant characteristics, flow and attrition rate

Of the 156 individuals who completed the pre-PE assessments and agreed to participate in the programme, 103 completed the post-PE assessments (66%). Twenty-nine patients (out of 156) did not have any data regarding the self-esteem measure because there was a delay in including this questionnaire in the protocol.

As shown in Figure 1, the 53 cases categorized as non-completers comprised of six individuals (4% of the total sample) who were referred for PE but were never able to commence therapy because of their level of depressive symptoms (MADRS score> 15); 19 individuals (12%) who missed >=2 PE sessions; and 24 PE completers (15%) who did not undertake the post-intervention assessments. Only 4 cases dropped out of PE because they experienced a BD relapse (mania=1; depression=3).

Baseline data showed that the mean age of the PE completers was about 42 years (S.D. 12) and mean duration of BD was about 16 years (S.D. 11); 58 of the completers were female (56%) and 75 had BD type 1 (73%). Also, 36 cases reported at least one suicide attempt (35%), and 63 had experienced psychotic symptoms during one or more BD episode(s) (61%;) only nine individuals reported no prior hospitalizations (9 %).

A comparison of the completers and non-completers (data not shown) revealed that the subgroups did not differ significantly on demography (age at participation p=0.44; sex-ratio p=0.24) or illness history (age at onset p=0.96; duration of illness p=0.70; percentage of BD type 1 p=0.38; history of psychotic features p=0.27; prior suicide attempt(s) p=0.25; hospitalisation rates p=0.43).

Table 1 reports the self- and observer ratings undertaken in PE completers and non-completers. As shown, the groups differed significantly in baseline levels of depressive symptoms, social functioning and illness perception.

Comparison of pre- and post-intervention scores for completers

As shown in Table 2, most measures improved during the group (anxiety trait, social functioning, knowledge about BD, illness perception, medication adherence, whereas others remained stable (MADRS, YMRS, anxiety state) or not significantly changed (self esteem). Regarding outcomes and potential mediators, most Effect Sizes (ES) for changes were small or medium (functioning, self-esteem, medication adherence, illness perception), except for change in knowledge about BD that was 1.2 (95% confidence intervals [CI]: 0.9, 1.49) (see table 2).

Associations between key outcomes and putative mediators

As change in one of the key outcome measures (self-esteem) was non-significant, further analyses were restricted to changes in social functioning. As shown in Table 3, improvement in social functioning was correlated with improvements in illness perception ($r=-0.29$; $p<0.003$), with a trend for an association with medication adherence ($r=-0.21$; $p<0.04$), but not knowledge.

The regression analysis demonstrated that the only variables reaching statistical significance in the model were baseline functional level (beta=0.54, 95% CI: 0.34, 0.65; t=6,4; p=0.0001), change in illness perception (beta=-0.29, 95% CI: -0.32, -0,07; t=3,1; p=0.002) and baseline value of illness perception (beta=-0,29 95% CI: -0.33, -0,06; t=-2.9; p=0.004). Results of the PROCESS model are presented in figure 1 and shows that only change in illness perception was associated to change in functioning (p=0,03) with no contribution (direct or indirect) of changes in adherence and knowledge about BD to change in functioning.

DISCUSSION

Group PE is a beneficial relapse prevention intervention for BD (Colom et al., 2003a; Colom et al., 2009), and can also be cost-effective (Parikh et al., 2012; Scott et al., 2009). However, like many evidence-based therapies, PE is routinely offered by less than 10% of the psychiatry services (Rummel-Kluge et al., 2013), and/or can fail to be translated into routine care (Roy-Byrne et al., 2003). Furthermore, there is a lack of data from generic services, and we identified only one published CER study that specifically examined the use of a structured PE group (Candini et al., 2013). Given the limited dissemination or lack of 'real-world data', we decided that a feasibility study

following the principles outlined by the IOM (1998) and NRC (2009) (Institute of Medicine, 1998; National Research Council, 2009) was both timely and important.

The study shows that most individuals with a primary diagnosis of BD who are referred to a PE programme can be included (<5% were unable to commence PE due to current symptoms). Attendance rates were high, with only 12% cases dropping out of PE because of missing two or more sessions (although another 15% failed to complete post-PE assessments). The baseline characteristics of non-completers indicated that they had significantly lower functioning, and more negative illness perceptions than completers and higher levels of depression. The latter is interesting as a common requirement for RCTs of PE is that cases are euthymic for several months prior to joining a group (Candini et al., 2013; Colom et al., 2009). Whilst sometimes viewed as overly restrictive, our study may indicate that this criterion has clinical validity. The non-completers in our sample were also characterized by less adaptive levels of illness perception at baseline. This observation is important as it suggests that the cases that clinicians identify as most likely to benefit from PE are at an above average risk of dropping out. Obviously, one clinical approach may be to offer additional pre-intervention appointments to these individuals, possibly incorporating motivational interviewing techniques to enhance their likelihood of engagement. Lastly, it is noteworthy that non-completers also showed greater impairment in social functioning compared to PE completers, which may support the view that functionally impaired BD cases might need to be directed towards other interventions such as functional remediation (Torrent et al., 2013).

For the PE completers, we observed improvements in one of the two key outcome measures (social functioning) and in dimensions that are targeted in PE interventions such as knowledge of BD, illness perception and medication adherence. The ES suggest that the magnitude of change was greatest for knowledge about BD and lowest for medication adherence, but the correlational and mediational analyses demonstrate that the clinical relevance of these changes is different. Namely, increase in knowledge showed no association with improved outcome (measured by functioning), or with more adaptive illness beliefs or medication adherence, confirming that change in knowledge alone is insufficient for improving outcomes in BD (Scott et al., 2012). The only potential mediator of the effectiveness of PE identified was change in illness perception. However, it met criteria as a partial not full mediator, so further studies will need to determine whether modulating perception and beliefs through an intervention that permitted both peer group and guided learning offers a sufficient but not necessary approach to reducing the illness burden (lower functioning and higher depression) and self-stigmatization (e.g. low self-esteem) associated with BD (Hawke et al., 2013; Latalova et al., 2013).

Our study has several limitations mainly linked to the quasi-experimental design such as the absence of a control group or blinding, although using self-reports minimizes the latter. (ii) We used a limited time period, as we were interested in patient-focused, subjective outcomes and early insights regarding the strengths and weaknesses of the programme rather than focussing on observer ratings of functioning or longer term relapse rate. (iii) Our intervention was shorter than the original group PE programme from Barcelona (20 *versus* 30 hours) (Colom, 2006). (iv) Other biases included the absence of details of prescribed medications, and lack of formal assessments of comorbidities, BD relapses or weekly symptom monitoring. (v) Whilst most of the instruments employed are well-established, the French 'Knowledge about BD' questionnaire is not yet validated. (vi) We cannot exclude a lack of power in our mediation analyses since our sample size might have been too small to detect significant indirect effects, although simulation studies indicate that the estimator of the standard error in simple mediation models (one or two mediators) might show low bias for sample sizes around 100 individuals (MacKinnon et al., 2007). (vii) It must be born in mind that, as well as sampling differences, this study focused on immediate benefits of PE after a short program. This may in part account for the more modest ES observed, as many experts in the field argue that patients might require more time to translate new knowledge or skills gained during PE into practical or observable changes in their lives, which in turn may mean downstream effects on functioning are not immediately recorded. Since no long-term prospective data were available for this sample, we cannot confirm or refute such suggestions, nor can we examine whether the changes in functioning are maintained over time. The ES for change in functioning in our study was 0.26 which is less than the 0.41 reported (Torrent et al., 2013) using the FAST (Functional Assessment Short Test) but greater than the 0.09 reported by (de Barros Pellegrinelli et al., 2013) using the GAF (Global Assessment of Functioning). These differences are likely to be a function of the instruments used for assessing changes in functioning, study methodologies and also the duration of follow-up, e.g. 12 weeks in our study versus 21 weeks in (Torrent et al., 2013). As previous studies have not assessed or not reported ES for self-esteem, illness perception changes in medication adherence, we cannot compare the magnitude of observed effects. However, our study does highlight the need to start to consider a broader range of outcomes (beyond symptoms or relapse) and to investigate putative mediators of the effects of PE and the similarities and differences in ES reported by studies employing different durations or types of PE. (viii) We chose broad inclusion criteria with very few exclusion criteria to increase the representativeness of the sample and the generalizability of the findings. This is in contrast to many RCTs that have employed eligibility criteria based on the minimal duration of euthymia prior to inclusion (e.g. 6-24 months) and/or excluded axis I or II comorbid psychiatric disorders or those individuals with any current or recent exposure to psychosocial interventions (Candini et al., 2013; Colom et al., 2003a; de Barros Pellegrinelli et al., 2013; Torrent et al., 2013).

Such studies are necessary to enable researchers to establish a 'signal' for the benefits of PE and other psychological interventions in BD, but can lead to the exclusion of up to 80% of the BD cases attending general psychiatry clinics (Scott et al, 2008). However, the use of less stringent criteria have increase the heterogeneity of the sample in our study and this may have led to false negative findings or attenuation of important effects.

Conclusions

Of those patients who started a 20-hour course of PE, more than two thirds completed >=80% of sessions and the pre- and post-PE assessments. The CER approach had strengths (rapid insights into dropouts, immediate outcomes and potential mediators), but also weaknesses (low intensity monitoring, reliance on self-rated assessments). Clinically, our 'real world data' illustrate that group PE is effective in improving social functioning and identifies the importance of further research on mediators. However, effect sizes for changes in our study remained low to moderate. Nevertheless, we found that illness perception might be important in differentiating PE completers from non-completers, showed significant pre- to post-PE change in the completer subsample and was the only putative mediator of the effect of PE on social functioning.

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Contributors
BE, JS and BC performed the analyses and wrote the paper.
BE, BC, FB and DF designed the psychoeducation programme.
BE, BC, CB, ND, SL, ID, LY and DF included and assessed the patients, and animated the psychoeducation sessions.
JRR and ML obtained the regulatory procedures, constructed and managed the database.
ML and CH revised the draft of the article.
All authors approved the final version of the article.

Conflicts of interest
None to be declared

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Bruno Etain is an Associate Professor of Psychiatry in the University Paris Diderot in France. He received his medical training and completed his psychiatric residency in France at the University Paris Descartes. In 2009, he achieved his Ph.D in Human Pathophysiology in the University of Paris East, working on genetic and environmental susceptibility factors to bipolar disorders. He is currently appointed as a visiting researcher during 2015-2019 at the centre for Affective Disorders (Pr AH Young), King's College of London, UK. Since 2008, he is one of the two coordinators of the FACE-BD network (FondaMental Advanced Centers of Expertise for Bipolar Disorders) that gathers 10 centre of expertise for Bipolar Disorders in France. Within the network, more than 2.500 patients with bipolar disorders have been assessed and have been included in a three years follow-up. He is in charge of the Centre of Expertise for Bipolar Disorders at Fernand Widal hospital in the center of Paris where he acts as a psychiatrist for bipolar patients, providing specialized consultations, medical expertise and psycho-education interventions for patients and caregivers. His main domains of research are : genetic factors, early environmental factors (mainly childhood trauma), circadian rhythms and response to lithium in bipolar disorders. He has contributed to more than 130 articles about bipolar disorders.

Figure 1: Flow chart of involvement in study of cases of bipolar disorder referred to group PsychoEducation (PE)

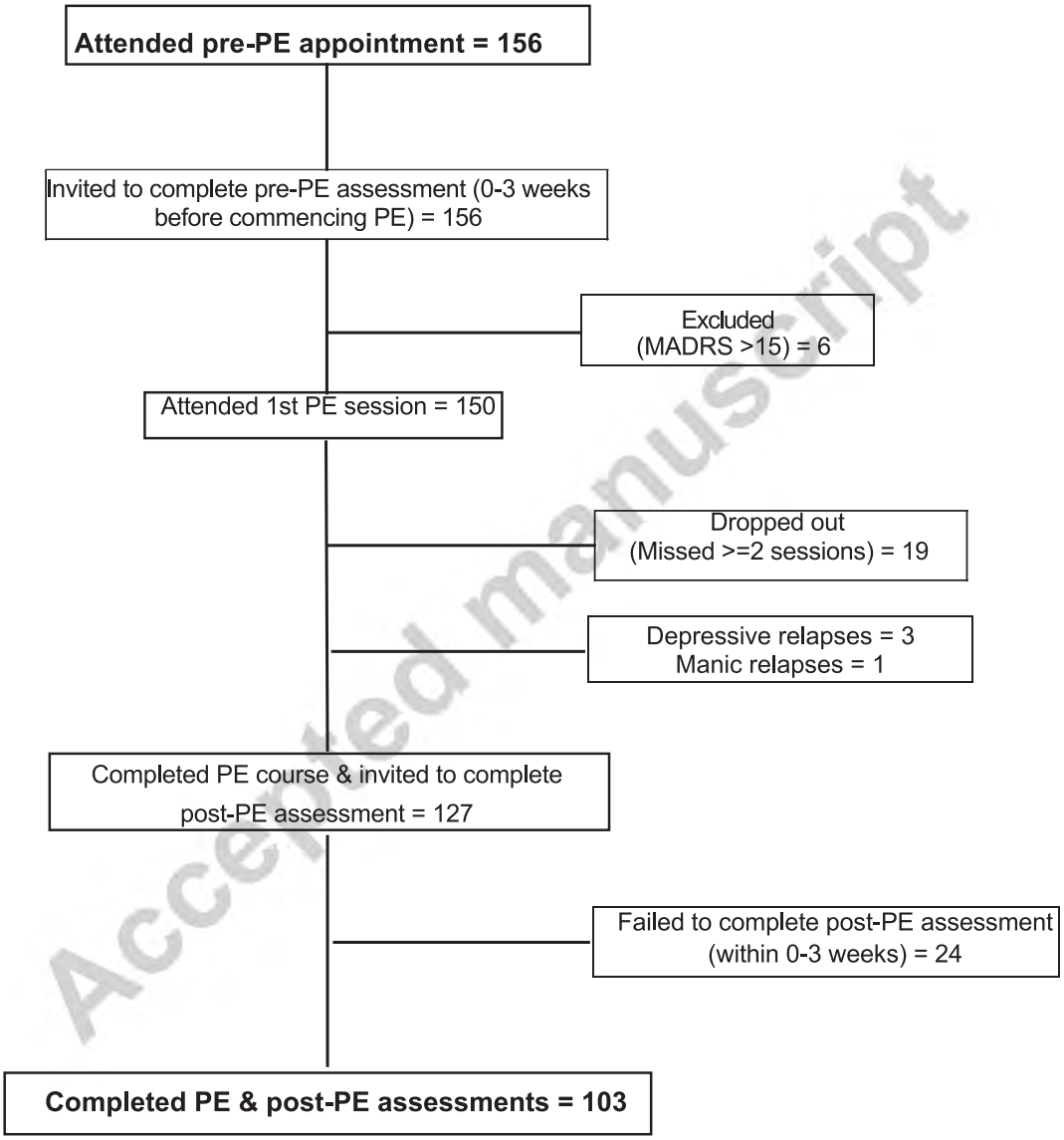
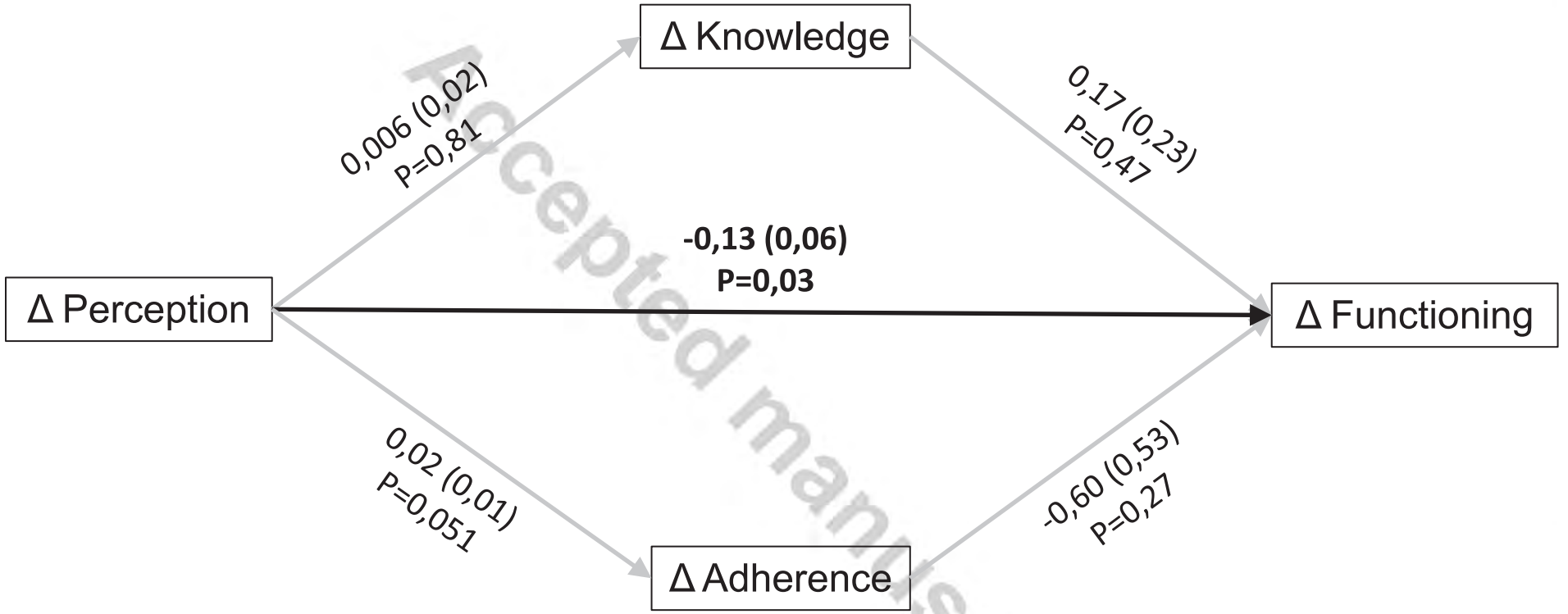


Figure 1: Path diagram of the mediation model



Δ Perception = change in illness perception; Δ Functioning= change in functioning

Change in knowledge in BD (Δ Knowledge) and change in adherence (Δ Adherence) are mediators (see text for details); Coefficients (standard errors) and p values are shown for each association.
Black arrows represent significant associations; Grey arrows represent non-significant associations

Table 1: Comparison of baseline assessment scores of PE completers and non-completers

Variables	Completers (n=103) N	Mean	SD	Non completers (n=56) N	Mean	SD	t	p
Symptoms:								
Depressive symptoms**	103	4.59	4.38	53	7.05	5.78	2.97	**0.003**
Manic symptoms**	103	0.62	1.06	52	0.81	1.35	0.93	0.35
Anxiety state	103	31.30	8.91	52	34.01	11.04	1.65	0.11
Anxiety trait	103	44.26	10.66	51	48.02	12.38	1.95	0.05
Key Outcomes:								
Social functioning [1]	102	62.02	7.98	52	57.23	9.24	-3.33	**0.001**
Self-esteem [2]	83	32.43	9.73	44	30.22	9.38	-1.23	0.22
Putative Mediators:								
Knowledge of BD [3]	103	13.73	3.10	53	12.80	3.40	-1.72	0.10
Illness perception [4]	102	41.70	11.17	52	46.92	10.91	2.76	**0.006**
Medication adherence [5]	101	2.01	1.47	51	2.52	1.84	1.86	0.06

**Bold type: statistically significant results after correction for multiple testing (p<0.009)*
1: a higher score indicates better functioning; 2: a higher score indicates higher self-esteem; 3: a higher score indicates better knowledge; 4: a lower score indicates more adaptive illness perception; 5: a higher score indicates better adherence;

***Median and Inter-quartile ranges:*
- for completers: MADRS 4.6 [1-8]; YMRS 0.6 [0-1].
- for non-completers: MADRS 7.1 [2-11]; YMRS 0.8 [0-1].

Table 2: Comparison of pre- and post-PE assessment scores of PE completers(n=103)

Variable	N	BEFORE		AFTER		t	df	p	Effect size (95%CI)
		Mean	SD	Mean	SD				
Symptoms:									
Depressive symptoms**	103	4.59	4.38	4.33	3.86	0.60	102	0.54	-0.06 (-0.33-0.21)
Manic symptoms**	103	0.62	1.06	0.88	1.71	-1.58	102	0.11	0.18 (-0.09-0.46)
Anxiety state	102	31.28	8.96	30.61	8.68	0.73	101	0.46	-0.08 (-0.35-0.20)
Anxiety trait	102	44.30	10.71	42.50	10.90	2.72	101	**0.007**	-0.17 (-0.44-0.11)
Key Outcomes:									
Social functioning	101	62.04	8.02	64.05	7.39	-3.00	100	**0.003**	0.26 (-0.02-0.54)
Self-esteem	82	32.37	9.78	33.67	9.15	-2.27	81	0.025	0.14 (-0,17-0.44)
Putative Mediators:									
Knowledge of BD	103	13.73	3.10	16.97	2.22	-11.64	102	**0.0001**	1.20 (0.90-1.49)
Illness perception	101	41.72	11.22	37.76	10.22	3.74	100	**0.0003**	-0.37 (-0.65--0.09)
Medication adherence	100	1.99	1.47	1.59	1.36	3.14	99	**0.002**	-0.28 (-0.56--0.01)

**Bold type: statistically significant results after correction for multiple testing (p<0.009)*

***Median and Inter-quartile ranges:*
- Before PE: MADRS 3 [1-8]; YMRS 0 [0-1].
- After PE: MADRS 4 [1-6]; YMRS 0 [0-1].

Table 3: Spearman correlations between pre- and post-PE changes in functioning and in knowledge, illness perception, and medication adherence in PE completers (n=103)

Pre-to-post PE change in scores		Δ Perception	Δ Knowledge	Δ Adherence
Δ Functioning	Rho	**-0.29**	0.08	-0.21
	signif. (p)*	**0.003**	0.41	0.04
Δ Perception	Rho		0.01	0.26
	signif. (p)*		0.89	**0.009**
Δ Knowledge	Rho			-0.04
	signif. (p)*			0.66

**Bold type: statistically significant results after correction for multiple testing*
Δ indicates the changes between pre- and post-PE scores

HIGHLIGHTS

More than 60% individuals completed a group psychoeducation programme.

Completers showed improvement in functioning but not self-esteem.

Change in illness perception mediated the change in functioning.

Changes in knowledge and adherence did not mediate the effects of psychoeducation.

Most effect sizes for changes were low to moderate.