

Correspondence

Edited by Kiriakos Xenitidis and
Colin Campbell

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Continuing lack of evidence for the psychotic subtyping of PTSD

Gaudiano & Zimmerman¹ conclude that psychotic symptoms in post-traumatic stress disorder (PTSD) are associated with comorbid conditions, especially major depressive disorders, and that their results therefore do not support the existence of a psychotic subtype of PTSD. However, they did not evaluate certain factors that might be responsible for misinterpretation of their results. First, they did not report the severity of post-traumatic and depressive symptoms. It is possible that patients with PTSD without comorbid depressive disorder had a milder post-traumatic disorder and consequently less probability of presenting with psychotic symptoms. Second, in clinical practice the congruence of delusions and hallucinations with traumatic events seems to be distributed across a continuum: at one extreme there is complete congruence with trauma and at the other there are exuberant and bizarre symptoms similar to those described in schizophrenia. The elucidation of the possible existence of a psychotic subtype of PTSD must necessarily include the development of adequate instruments to measure severity and congruence of psychotic symptoms in 'non-psychotic' conditions (e.g. mood and anxiety disorders), as well as their biological correlates.

- 1 Gaudiano BA, Zimmerman M. Evaluation of evidence for the psychotic subtyping of post-traumatic stress disorder. *Br J Psychiatry* 2010; **197**: 326–7.

Elisa Brietzke, Associate Researcher, Department of Psychiatry, Federal University of São Paulo, São Paulo, Brazil, email: elisabrietze@hotmail.com; **André Zugman**, **Elson Asevedo**, **Rodrigo Mansur**, **Gracielle Rodrigues da Cunham**, Department of Psychiatry, Federal University of São Paulo, São Paulo, Brazil

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Authors' reply: We welcome the response by Brietzke and colleagues to our report. First, they suggest that differences in illness severity between those with *v.* those without the comorbidities we excluded might have accounted for reductions in the prevalence rate of psychotic symptoms in our sample. To help address this point, we reanalysed our data by conducting a logistic regression of data for PTSD patients with *v.* without the excluded comorbidities as a predictor of the likelihood of having psychotic symptoms while controlling for Global Assessment of Functioning scores. Comorbid status remained a significant predictor. It is important to clarify we did not exclude all comorbidities from the PTSD sample: we removed only those that also allow for the presence of psychotic symptoms (e.g. schizophrenia, bipolar disorder). Other comorbid diagnoses

(e.g. anxiety disorders) remained in the refined PTSD sample showing the low prevalence of psychosis. Therefore, we do not believe that differences in illness severity can adequately explain our findings.

Second, Brietzke *et al* point out that psychotic symptoms in PTSD probably fall along a spectrum from congruent (e.g. hallucinations related to vivid re-experiencing of the trauma) to non-congruent (e.g. bizarre, non-trauma-related hallucinations). We agree with this observation in general, but disagree that congruence criteria are likely to clarify these issues from a diagnostic standpoint. The distinction between congruent *v.* non-congruent psychotic symptoms in primary mood disorders is known to lack prognostic value and patients frequently exhibit characteristics of both at the same time.¹

We agree with Rosen & Lilienfeld² that continued conceptual confusion regarding the PTSD diagnosis suggests the need for greater caution, rather than a rush to expand the criteria to encompass larger groups of clinical presentations, until the validity of the core features of the PTSD diagnosis can be better established. We also disagree with Brietzke *et al* that investigations of biological correlates of PTSD are likely to shed much more light on these issues. Extensive previous research in this area has found a lack of evidence for biomarkers linked specifically to the PTSD diagnosis as opposed to those that cut broadly across diagnostic categories and clinical presentations.²

- 1 Gaudiano BA, Uebelacker LA, Miller IW. Course of illness in psychotic mania: is mood congruence important? *J Nerv Ment Dis* 2007; **195**: 226–32.
2 Rosen GM, Lilienfeld SO. Posttraumatic stress disorder: an empirical evaluation of core assumptions. *Clin Psych Rev* 2008; **837**: 837–68.

Brandon A. Gaudiano, Psychologist, Alpert Medical School of Brown University, and Butler Hospital, Providence, Rhode Island, email: Brandon_Gaudiano@brown.edu; **Mark Zimmerman**, Alpert Medical School of Brown University, and Department of Psychiatry, Rhode Island Hospital, Providence, Rhode Island, USA

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Is transference-focused psychotherapy really efficacious for borderline personality disorder?

In their study of treatment for borderline personality disorder, Doering *et al* state that their results 'demonstrate the significant superiority of transference-focused psychotherapy with regard to the primary outcome criteria of drop-out rate and suicide attempts during the treatment year' when compared with treatment by experienced community psychotherapists.¹ They report that 'significantly fewer participants dropped out of the transference-focused psychotherapy group (38.5% *v.* 67.3%) and also significantly fewer attempted suicide ($d = 0.8$, $P = 0.009$)'.

In our view, this interpretation of primary outcome criteria might lead to misunderstandings. As regards suicidality, the authors suggest that the P -value of 0.009 would relate to absolute numbers of attempted suicides during the treatment year. However, the actual difference in suicide attempts during the treatment year (7/52 *v.* 11/52) is not significant ($P = 0.44$, continuity-corrected χ^2 -test, LOCF analysis). The significant P -value reported by the authors seems to correspond to change scores (defined as $1/0 - 1$ by the authors), not to suicide attempts during the treatment year, which seems to be the outcome as defined in the study protocol (trial NCT00714311). The authors further suggest that the effect size of 0.8 would refer to the between-group comparison. However, the reported effect size seems to correspond to the within-group comparisons reported in Table DS2. The between-group effect size for suicide attempts during the treatment year would be small.

The other primary outcome to assess efficacy was defined as the rate of participants not receiving the allocated treatment plus the rate of participants who discontinued the allocated treatment. Even when accepting that patients not even starting treatment were included in a measure of treatment efficacy, it seems problematic to ascribe differences in this criterion to the efficacy of transference-focused psychotherapy without excluding accumulative effects of alternative explanations. The higher rate of non-starters among patients randomised to community therapists (the control condition) compared with those randomised to transference-focused psychotherapy (25% *v.* 13%) and the substantially higher rate of patients stopping treatment in the control group within the first month (Fig. 2 of the paper) might reflect a general preference of participants for transference-focused psychotherapy rather than its superior efficacy. Furthermore, the authors have not mentioned that this criterion combining non-starters and ‘drop-outs’ as primary outcome of efficacy was introduced *post hoc* (for *post-hoc* changes in the definition of primary outcome criteria see <http://clinicaltrials.gov/archive/NCT00714311>). Without addressing this issue, the statistical implications of this proceeding are difficult to evaluate.

As for the secondary outcome measures, the picture seems to be mixed. Some of the LOCF analyses indicated lower scores after transference-focused psychotherapy (e.g. number of borderline criteria, level of personality organisation). Other scores (e.g. general psychopathology, depression) were numerically higher after transference-focused psychotherapy and did not improve significantly more under it ($P=0.92$ and $P=0.85$ for general psychopathology and depression respectively).

Recapitulating, it seems that the claimed efficacy of transference-focused psychotherapy does not follow from the primary outcome criteria. Accordingly, further research seems necessary to establish the efficacy of this therapy in the treatment of borderline personality disorder.

- 1 Doering S, Hörz S, Rentrop M, Fischer-Kern M, Schuster P, Benecke C, et al. Transference-focused psychotherapy *v.* treatment by community psychotherapists for borderline personality disorder: randomised controlled trial. *Br J Psychiatry* 2010; **196**: 389–95.

Nikolaus Kleindienst, Department of Psychosomatic Medicine, Central Institute of Mental Health, J5, D-68159 Mannheim, Germany, email: Nikolaus.Kleindienst@zi-mannheim.de; **Bertram Krumm**, Department for Biostatistics, **Martin Bohus**, Department of Psychosomatic Medicine, Central Institute of Mental Health, Mannheim, Germany

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Author’s reply: Kleindienst and colleagues argue that our interpretation of the treatment outcome with regard to suicide attempts might lead to misunderstandings. They are right that a χ^2 -test comparing the absolute number of suicide attempters in both groups, transference-focused psychotherapy and treatment by experienced community psychotherapists, is not significant. However, this test does not seem appropriate in the present context, since the baseline, that is the number of suicide attempters during the year before treatment, was not equal in both groups (18 in the transference-focused psychotherapy group *v.* 12 in the community psychotherapists group). Thus, a statistical approach had to be employed that controls for baseline data. Since no χ^2 -test exists that controls for baseline values, we defined change scores that allow for baseline control within a Mann–Whitney U-test. This test generated the $P=0.009$ that, in our opinion, depicts the real changes in suicide attempters in both groups. A between-group effect size of 0.55 for the time \times group

interaction in suicide attempts was calculated from the χ^2 -statistics of the change scores ($\chi^2=7.126$, d.f.=2, $P<0.028$). Table DS2 of our paper only reports within-group effect sizes; between-group effect sizes were not calculated.

The issue of treatment drop-out is a limitation of this study, which has been thoroughly controlled for and discussed in our paper. After the decision to use treatment drop-out as a primary outcome criterion, we preferred to keep strictly to the intent-to-treat algorithm that demands every randomised patient to be part of the outcome analysis. Nevertheless, to address the understandable criticism raised by Kleindienst and colleagues, we repeated the drop-out analysis after excluding from it patients who did not begin therapy after randomisation. This analysis still revealed a significantly lower number dropping out of the transference-focused psychotherapy group (15 *v.* 23; $\chi^2=5.750$, d.f.=1, $P=0.016$).

The changes in the primary outcome criteria had been made following the impression of an ongoing discussion in the literature addressing the adequacy of DSM–IV diagnostic criteria as outcome criteria in treatment studies.^{1,2} Since our initial outcome criteria ‘number of DSM–IV borderline criteria’ and ‘GAF score’ revealed an even stronger superiority of transference-focused psychotherapy, we did not report this *post-hoc* change, because a bias in our decision was not suspected.

We thank Kleindienst and colleagues for their criticism and the Editor for giving us the opportunity to clarify important issues regarding our study. We hope that our comments will eliminate doubts concerning the fact that our study documents the efficacy of transference-focused psychotherapy for the treatment of borderline personality disorder.

- 1 Skodol AE, Pagano ME, Bender DS, Shea MT, Gunderson JG, Yen S, et al. Stability of functional impairment in patients with schizotypal, borderline, avoidant, or obsessive–compulsive personality disorder over two years. *Psychol Med* 2005; **35**: 443–51.
- 2 Zanarini MC, Frankenburg FR, Reich DB, Silk KR, Hudson JI, McSweeney LB. The subsyndromal phenomenology of borderline personality disorder: a 10-year follow-up study. *Am J Psychiatry* 2007; **164**: 929–35.

Stephan Doering, Department of Psychoanalysis and Psychotherapy, Medical University of Vienna, Austria, email: Stephan.Doering@ukmuenster.de

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Ziprasidone and the relative risk of diabetes

Kessing *et al*¹ describe the risks of diabetes in clinical practice from a large-cohort, observational study of Danish patients requiring antipsychotics. We believe that the relative risks of subsequent incident diabetes that they report for individual antipsychotics are at odds with established literature. The preponderance of evidence has demonstrated that ziprasidone has limited effect on metabolic indices associated with the development of diabetes. We present some of that evidence below.

In the CATIE study of 1493 patients with schizophrenia receiving olanzapine, quetiapine, risperidone, ziprasidone or perphenazine for up to 18 months, ziprasidone was the only drug associated with improvement in glycosylated haemoglobin, total cholesterol and triglycerides. Meyer and colleagues² reported that, in the CATIE trial, the prevalence of metabolic syndrome increased for olanzapine (from 34.8% to 43.9%) but decreased for ziprasidone (from 37.7% to 29.9%), and that the comparison between ziprasidone and olanzapine was statistically significant ($P=0.001$).

In the EUFEST study of 498 patients with first-episode schizophrenia assigned to haloperidol, amisulpride, olanzapine,