Comment

Psychopathology

Psychopathology 2017;50:228–230
DOI: 10.1159/000477371

Received: May 7, 2017
Accepted after revision: May 10, 2017
Published online: June 10, 2017

Rejoinder to Commentary: "Panic, Self-Disorder, and EASE Research: Methodological Considerations"

Luís Madeira[a, b] Sergio Carmenates[a] Cristina Costa[c] Ludgero Linhares[a]
Giovanni Stanghellini[d, e] Maria Luísa Figueira[b] Louis Sass[f]

[a]Psychiatry Department, Centro Hospitalar Lisboa Norte, [b]Faculdade de Medicina, Universidade de Lisboa, and [c]Centro Hospitalar Psiquiátrico de Lisboa, Lisbon, Portugal; [d]Department of Humanistic, Health and Territorial Sciences (DISPUTER), "G. d'Annunzio" University, Chieti, Italy; [e]"D. Portales" University, Santiago, Chile; [f]Graduate School of Applied and Professional Psychology, Rutgers University, Piscataway, NJ, USA

Our aim in this rejoinder is to reply to the comment by Parnas et al. [1] on our recent paper in *Psychopathology* on self-disorders in panic disorder (PD) [2]. Their comment makes a series of incorrect or misleading claims.

The comment starts by stating that our sample is "*chronic*" and "*treatment-resistant*" and that we aimed to compare our PD subjects' scores with the scores of schizophrenia subjects. Both claims are incorrect. Our sample is not, in fact, especially *chronic* given that *recurrent* panic attacks are actually *a criterion* for the very diagnosis of PD [3]. Nor does failure of a 1-month treatment in General Practice Clinics (also characteristic of our subjects) qualify as clinical *treatment resistance*. The general remission rate of PD in general is 80% in the second year of treatment [4, 5], and perhaps only at that point should patients be considered *resistant*.

Contrary to what the comment implies, our study was not devised to provide a direct comparison of patient groups; for that we would have had to include *both* PD and schizophrenia samples. Our aim, rather, was to examine the presence, and the profile, of self-disorders in PD: "*to explore the profile of specific types of ASEs (…) any possible patterns (…) that might be revealed*" [2]. The comment also criticizes our consideration of all the 94 EASE items or sub-items rather than only the 57 items (only some of which have sub-items). But given our purposes, maximum qualitative detail was critical, since our main purpose involved seeking the richest possible phenomenological assessment. We have, however, reanalyzed our data using only the 57 EASE items, and this leads to an average score of 13.11 ± 8.8 (mean ± SD), versus our initial 17.94 ± 11.88. We regret that we did not include this analysis in our original paper. However, using this result does not change our discussion, namely, that our scores are indeed "*somewhat lower than (schizophrenia studies) but considerably higher than those reported for bipolar psychosis (average of 6.3) and other mental disorders (average of 8.1) in the just cited comparative studies*."

The commentary suggests that PD is a "trans-diagnostic category" (in contrast with our claim that some *self-disorders* could be trans-diagnostic), whose presence in our sample would increase the odds ratio of a future diagnosis of psychosis. This suggestion contradicts the best available epidemiological evidence, which indicates that PD, despite its comorbidities, is a stable diagnostic category [6]. We note also that our own sample is not (as they claim) "peculiar" in lacking comorbidities since it was intentionally *selected* on that very basis (with inclusion criterion "diagnosis of panic disorder and no other diagno-

E-Mail karger@karger.com
www.karger.com/psp

Luís Madeira
Faculdade de Medicina, Universidade de Lisboa
Av. Prof. Egas Moniz
PT–1649-035 Lisbon (Portugal)
E-Mail luismadeiramd@gmail.com

sis" [2]). Likewise, it is highly implausible to suggest that past and present panic attacks (defined as involving sudden physical and psychical anxiety with *fear of* losing control and help-seeking behavior) could be mistaken by trained psychiatrists, in a clinical setting, with actual psychotic episodes (delusions and hallucinations with possible disorganized speech and behavior). Also, the most recent epidemiological study (which includes Portuguese subjects in its sample) shows high comorbid diagnosis of PD with "other anxiety disorders (63.1%) and mood disorders (53.7%)" but *not* with psychosis [6]. The latter study also refutes the idea that PD *precedes* comorbid psychosis, given that it is rare for the PD diagnosis to *precede the comorbid diagnosis* (only 15.4% of this already rare subgroup) [6].

Two other methodological criticisms in the comment claim (1) that our clinical assessment was inadequate since it relied on the M.I.N.I. International Neuropsychiatric Interview (5.0) [7] and (2) that we failed to consider or properly assess the possible co-presence of schizophrenia spectrum conditions. However, as we stated, our subjects were assessed *not only* with the M.I.N.I but also with *two additional* diagnostic clinical interviews performed by licensed university clinic psychiatrists (at admission, and also on referral to our research team); the M.I.N.I. was an *additional* device used only to exclude certain specific psychiatric diagnoses (particularly affective disorders). It is also odd to find the commentators suggesting we somehow ignored the possibility of comorbid schizophrenia spectrum conditions, given that we addressed this issue repeatedly. Indeed, "schizophrenia spectrum" is mentioned 31 times in our paper, including the possibility (which we consider highly unlikely) of failing to detect what we term the "presence, in some PD subjects, of subclinical schizotypal or other psychosis-prone traits."

The last two criticisms in the comment refer to (1) the nonblindness to diagnosis of our interviewers and (2) a supposed lack of "certification" to perform the EASE. The interviews were performed by licensed and experienced psychiatrists who intentionally refrained from asking about the diagnosis of the interviewee. The course of the interview does, however, solicit biographical and clinical information that can be relevant to diagnostic considerations (e.g., whether EASE sub-items occur only in specific settings and/or acute mental states or as trait-like features present from childhood or adolescence). We certainly agree with the commentators that complete diagnostic blindness was impossible "given the intensity, depth and breadth" of the [EASE] interview. This, however, is the case *for any EASE interview whatsoever*, and is therefore no more problematic in our interviews than for *all* previous and future research with the EASE. We fail to see what point our commentators are trying to make on this issue.

Another incorrect point is the commentators' claim that our interviewers (together with numerous other researchers) lacked "certification" and training as they did not go through a "long, arduous training of several months." This seems a dubious attempt to impugn the carefulness and rigor of our research. Our interviewers did, in fact, take the official EASE courses that were recommended before and at the time of the study (these were promoted by the Centre for Subjectivity Research [CfSR] in Copenhagen, and taken by our interviewers in 2013 and 2015.) Further, our interviewers performed hundreds of EASE interviews in these and other research settings, where reliability has also been appraised [8, 9]. We agree that training and reliability assessments can increase the excellence of interview(er)s and we appreciate the introduction of a new *advanced EASE workshop* and *reliability appraisal* in the www.easenet.dk website. It is noteworthy, however, that this suggestion has appeared only recently on the EASE website (well after our research was performed) – a point that, in all fairness, should have been mentioned by the commentators.

At the same time, we wish to point to some worrisome methodological problems that could ensue from too local or too parochial a monitoring of EASE training, e.g., only by any group that might be unduly biased toward associating self-disorder *per se* only with schizophrenia spectrum. The danger is that a tautological or self-perpetuating orientation might prevail, especially given the difficulty of achieving full diagnostic blindness in an interview like the EASE. We are referring to a situation in which trainees who wish to be qualified to perform EASE interviews might feel some pressure to find EASE items only in subjects who seem likely to have a schizophrenia diagnosis (we are assuming, of course, that such pressure would only be indirect and unintentional; such pressures are, however, known to have significant effects in scientific research, especially when considerable judgment is required, as when assessing subtle experiential phenomena). In this light, we cannot help but notice that the authors of the comment sometimes seem to verge (at least in our view) on actually *defining* schizophrenia in terms of the presence of EASE items and self-disorders. This, of course, would mean adopting a tautological and therefore scientifically untenable position, a position in which it would be virtually impossible, *on principle*, to find results conflicting with the following claim (which is incorrect in

our view, though it is repeated in various publications by the commentators): namely, that "it has now been established empirically that self-disorders aggregate in schizophrenia-spectrum disorders but not in other mental disorders or in healthy controls" [10].

To claim that self-disorders aggregate *only* in schizophrenia spectrum, and not in any other disorders, it would be necessary to make comparisons *not* merely with affective-disorder or *general* psychiatric samples but with *most* or many other *specific* psychiatric disorders outside the schizophrenia spectrum (beyond that which has been done by the Copenhagen Group). High prominence of self-anomalies was in fact already found in a prior, EASE-based study (only quasi-empirical) of depersonalization disorder [11], in cases of intense introspection [12] and, more broadly, in phenomena from avant-garde modernist and postmodernist art and culture [13]. This is hardly surprising, perhaps, given the prominence of derealization or depersonalization in such disorders as PTSD, depersonalization disorder, and some additional anxiety disorders. As we note, 13 EASE sub-items are more or less identical with Cambridge Depersonalization Scale (CDS) items, while 11 other EASE items have close affinity [14].

Our own position is very much in favor of the self-disorder hypothesis of schizophrenia. However, we believe that to progress in studying self-disorder in schizophrenia, one must critically explore notions of basic-self and its disturbances, and investigate significant parallels and affinities with certain other disorders. Pathogenesis of full-blown schizophrenic symptoms might require, as has been suggested, a 2-tier (and specific) construal of experiences [15]. Another plausible model interprets self-disorders in schizophrenia in light of a 2-factor theory, with disturbed ipseity having (at least) 2 sources: one involving neurobiologically grounded forms of perceptual dys-integration, the other involving largely defensively driven forms of depersonalization and derealization akin to trauma response. Schizophrenic self-disorder would be understood as the joint product of both these factors, both being necessary but neither sufficient [16, 17]. Such a view is consistent with the now widely acknowledged role of stress and trauma in the etiology of schizophrenia [18, 19].

Everyone recognizes that scientific progress requires the respectful consideration of opposing findings. In this spirit, we note that, in our manuscript, we certainly do not ignore, but actually *raise* a variety of *possible objections* to our findings – a point that seems to have been lost on the commentators. Far from bringing *confusion* into this research field, we believe that studies such as ours offer necessary refinements that will ultimately lead to a more nuanced and more adequate conception of the nature and internal structure of ipseity or "basic-self" and its disorders.

References

1 Parnas J, Nordgaard J, Henriksen MG: Panic, self-disorder, and ease research: methodological considerations. Psychopathology 2017;50:169–170.
2 Madeira L, Carmenates S, Costa C, Linhares L, Stanghellini G, Figueira ML, et al: Basic self-disturbances beyond schizophrenia: discrepancies and affinities in panic disorder – an empirical clinical study. Psychopathology 2017;50:157–168.
3 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). Arlington, APA Publishing, 2013.
4 Cloos J-M: The treatment of panic disorder. Curr Opinion Psychiatry 2005;18:45.
5 Choy Y: Treatment planning for panic disorder: evidence-based treatments. Psychiatr Times 2008;25:40.
6 Jonge P, Roest AM, Lim CCW, Florescu SE, Bromet EJ, Stein DJ, et al: Cross-national epidemiology of panic disorder and panic attacks in the world mental health surveys. Depress Anxiety 2016;33:1155–1177.
7 Lecrubier Y, Sheehan D, Hergueta T, Weiller E: The mini international neuropsychiatric interview. Eur Psychiatry 1998;13:198s.
8 Madeira L, Bonoldi I, Rocchetti M, Brandizzi M, Samson C, Azis M, et al: Prevalence and implications of Truman symptoms in subjects at ultra high risk for psychosis. Psychiatry Res 2016;238:270–276.
9 Madeira L, Bonoldi I, Rocchetti M, Samson C, Azis M, Queen B, et al: An initial investigation of abnormal bodily phenomena in subjects at ultra high risk for psychosis: their prevalence and clinical implications. Compr Psychiatry 2016;66:39–45.
10 Nordgaard J, Handest P, Vollmer-Larsen A, Sæbye D, Pedersen JT, Parnas J: Temporal persistence of anomalous self-experience: a 5 years follow-up. Schizophr Res 2017;179:36–40.
11 Sass L, Pienkos E, Nelson B, Medford N: Anomalous self-experience in depersonalization and schizophrenia: a comparative investigation. Conscious Cogn 2013;22:430–441.
12 Sass L, Pienkos E, Nelson B: Introspection and schizophrenia: a comparative investigation of anomalous self experiences. Conscious Cogn 2013;22:853–867.
13 Sass LA: Madness and Modernism. New York, Basic Books, 1992.
14 Sierra M, Berrios GE: The Cambridge Depersonalization Scale: a new instrument for the measurement of depersonalization. Psychiatry Res 2000;93:153–164.
15 Stanghellini G, Rosfort R: Disordered selves or persons with schizophrenia? Curr Opin Psychiatry 2015;28:256–263.
16 Borda JP, Sass LA: Phenomenology and neurobiology of self disorder in schizophrenia: primary factors. Schizophr Res 2015;169:464–473.
17 Sass LA, Borda JP: Phenomenology and neurobiology of self disorder in schizophrenia: secondary factors. Schizophr Res 2015;169:474–482.
18 Bendall S, Jackson HJ, Hulbert CA, McGorry PD: Childhood trauma and psychotic disorders: a systematic, critical review of the evidence. Schizophr Bull 2008;34:568–579.
19 Renard SB, Huntjens RJ, Lysaker PH, Moskowitz A, Aleman A, Pijnenborg GH: Unique and overlapping symptoms in schizophrenia spectrum and dissociative disorders in relation to models of psychopathology: a systematic review. Schizophr Bull 2017;43:108–121.