Valproic Acid and Hypersensitivity Syndrome

TO THE EDITOR: Hypersensitivity syndrome is a rare but potentially life-threatening adverse drug reaction that occurs 2 to 6 weeks after exposure to, most commonly, aromatic anticonvulsants. The clinical picture is characterized by a triad of fever, skin rash (almost 100% of the skin's surface, ranging from mild exanthema to toxic epidermal necrolysis), and organ involvement (50% liver, 11% kidney). Lymphadenopathy (75%) and eosinophilia (30%) are frequent (1). The pathogenesis is not clear. Cross-reactivity has been observed among aromatic anticonvulsives, whereas nonaromatic drugs, such as valproic acid, are often recommended in these cases. We located only three cases of hypersensitivity syndrome induced by valproic acid for nonpsychiatric use (2–4).

Mr. A, a 48-year-old man, had been diagnosed with schizoaffective disorder 30 years previously and had been treated with haloperidol, fluphenazine, promethazine, and biperiden. He was admitted to a psychiatric hospital with schizomanic syndrome and was treated initially with oral haloperidol, fluphenazine, diazepam, clomethiazole, promethazine, biperiden, and vitamins B_1 and B_6. On day 3, his therapy was switched to prolonged-release oral valproic acid, amisulpride, and lithium; administration of vitamins B_1 and B_6 was continued.

Three weeks after initiation of therapy, Mr. A developed a generalized maculopapular rash with lymphadenopathy and fever (39.1°C); his total WBC count was 14.2 cells/nl, and his levels of transaminases and creatinine were slightly elevated.

We discontinued valproic acid and vitamins B_1 and B_6 after diagnosing a severe adverse drug reaction presenting as hypersensitivity syndrome. We introduced olanzapine with prednisolone (initially 80 mg/day). The skin rash as well as other clinical symptoms (including an intermittently elevated WBC count of 37.9 cells/nl with maximal eosinophilia of 24%) remitted completely in the next week. Therapy with corticosteroids was tapered over 3 weeks. After release from the hospital, Mr. A remained stable over the following 3 months while taking olanzapine, amisulpride, and lithium.

A skin patch test performed at 3 months to test for valproate and vitamins B_1 and B_6 (pure and 30% in distilled water, respectively) gave a positive reading for the valproic acid preparations at 72 hours, while three healthy volunteers were negative for these compounds.

To our knowledge, this is the first report of a hypersensitivity syndrome induced by valproic acid in a psychiatric patient. The positive skin patch test confirmed the diagnosis (5). Our observation underlines the fact that valproic acid, a nonaromatic anticonvulsant, may also lead to severe adverse reactions.

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Pitfalls in Factor Analytic Techniques

TO THE EDITOR: We read with great interest the article by John P. Alsobrook II, Ph.D., and David L. Pauls, Ph.D. (1), in which they used factor analytic techniques to reveal underlying structures in Gilles de la Tourette's syndrome. The main applications of factor analytic techniques are to reduce the number of variables and to detect structure in the relationship among variables. We want to point out some pitfalls that go along with the use of factor analysis in general and the application of Drs. Alsobrook and Pauls in particular.

A preliminary step in factor analysis is the determination of the number of factors one wishes to retain. Drs. Alsobrook and Pauls applied the widely used Kaiser rule (eigenvalues >1). Zwick and Velicer (2) compared five different methods for the determination of the number of factors and demonstrated that use of this rule consistently leads to an overestimation of the number of factors. An alternative method of determining the number of factors may be combination of the Kaiser rule with inspection of the scree plot.

After factor analysis, rotational strategies (e.g., varimax) can be used to obtain a clear pattern of loadings. An orthogonal method of rotation, such as the varimax rotation used by Drs. Alsobrook and Pauls, requires that the resulting factors do not correlate. The appropriateness of this method is questionable since symptoms in psychiatric syndromes may inherently show a certain degree of correlation. Oblique rotation (in which factors are allowed to correlate) should be considered since oblique rotation methods produce orthogonal solutions, if appropriate (3).

Loadings are simply correlations between an item and a factor; therefore, they need to be statistically significant, and consequently, group size should be taken into account. Drs. Alsobrook and Pauls used an absolute value of 0.200 as a threshold for the interpretation of factor loadings. According to Stevens (4), a group size of 670 patients would be required for such a threshold. Drs. Alsobrook and Pauls included 85 patients, a group size that allows loadings of merely >0.556. Anyhow, regardless of the group size, loadings with values of 0.200 explain only as little as 4% of the shared variance between an item and a factor.

Statistical software packages such as SPSS offer default options for performing factor analyses. A principal components analysis with varimax rotation based on eigenvalues >1, used by Drs. Alsobrook and Pauls, is an example of such a standardized option. Unfortunately, when followed too obediently, these options may seriously compromise research data.

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Learning and Brain Function in Schizophrenia

TO THE EDITOR: The positron emission tomography (PET) imaging study of deficit and nondeficit patients with schizophrenia and healthy volunteers conducted by Adrienne C. Lahti, M.D., and colleagues (1) revealed statistically significant mean differences among these groups in certain brain areas. However, two important points were not discussed by the authors, and these issues challenge the view that the authors' work supports the hypotheses regarding putative brain areas relevant to the distinction between deficit and nondeficit schizophrenia.

1. Given their use of categorical differentiation of the three groups by diagnostic and negative symptom assessments and the statistically different mean differences among these groups, how do the authors explain the striking and graphic overlapping of the distributions of both pretask and posttask differences and the direction of changes, as displayed so clearly in their Figure 1?

2. The authors found no differences in the learning of the tone-discrimination task among the three conditions; all three groups reached high levels of accuracy in the training procedure. Therefore, to what compensatory brain mechanisms do the authors attribute these similarities in performance across groups in the face of the differences found in the hypothesized—but few—brain areas? If the learning and performance of these three groups were equally good, there would appear to be either 1) some compensatory processes or brain regions that function well to compensate for the hypothesis-driven impairments found in a few brain areas or 2) the hypothesis-driven brain areas that were found to be deficient in the schizophrenia groups were unrelated to the performance on the auditory recognition and discrimination tasks used by the authors.

For me, the most important findings from the study were those noted in these two points. A thoughtful exchange with the authors on the interpretation of their results would help to elucidate further the purported relations between learning and brain function, as measured by the particular PET imaging technique used by Dr. Lahti and her colleagues.

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Cognitive Decline in Preschizophrenia Patients

TO THE EDITOR: We read with interest the article by Rebecca Fuller, Ph.D., et al. (1) that concluded that significant cognitive decline occurred in preschizophrenic patients, accounting for the deterioration in academic grades between the ages of 13 and 16 years. We conducted a preliminary case-control study in Singapore with a uniform group of 30 first-episode schizophrenia patients with illness onset at age 20 years who were without a past psychiatric or substance use history. They were compared with 30 normal subjects who were closely matched for sex, age, and academic results at age 12. We found that academic decline, as documented on standardized national examinations, also occurred between ages 12 and 16 years, some 3 to 8 years before schizophrenia onset (2).

Indeed, the conclusions about preschizophrenic cognitive decline in the study by Dr. Fuller et al. (1) could be stronger if information were available to exclude other confounders of academic functioning, such as comorbid conduct, substance use, or other psychiatric disorders, as well as the contribution of other prodromal symptoms. While the contribution of prodromal symptoms was dismissed on the basis of finding of no correlation between age at illness onset and test scores, there may not be simple relationships between them. For example, test scores at grade 11 could be confounded by earlier scores, premorbid intelligence, and psychiatric comorbidities. Previous studies of prodromal symptoms of first-episode psychosis point to the presence of a variety of emotional and attenuated negative symptoms (3, 4), all of which also could contribute to the academic decline observed. Nevertheless, these appeared less likely, since despite limitations of recall in these retrospective studies, it appeared from detailed interviews with patients and informants that cognitive disturbances (disturbances in attention, concentration, or memory and deterioration in school results), rather than neurotic symptoms, were more specific to the psychotic prodrome and that cognitive symptoms appeared to be the first manifestation (4).

Indeed, the analysis of results from widely administered standardized school examinations at various ages, like that reported by Dr. Fuller and colleagues (1), represents a useful approach that, combined with more information on emotional and other functioning at those times, could yield valuable insights into the preschizophrenic process that in the future may lend themselves to early detection and intervention.

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Dr. Fuller and Colleagues Reply

TO THE EDITOR: We thank Drs. Tan and Ang for their insightful remarks. It is interesting to hear that a similar decline in scholastic test results has been documented in a group of patients in Singapore. We appreciate the suggestions made for obtaining stronger conclusions and would like to address these. The scholastic test scores reported in this study were obtained directly from the agency that administered the standardized testing. These scores were assessed before illness onset, when no one had knowledge about the future development of schizophrenia. We feel that this is the main strength of our study since, unlike data obtained from patients or other informants after the diagnosis of schizophrenia, these test scores were not subject to recall bias. For the current study, we did not have any reports from teachers regarding conduct. We did not systematically collect childhood psychiatric records because most of our patients never required psychiatric treatment before the onset of schizophrenia. Indeed, test scores at grade 11 may be confounded by earlier scores, but we reported the scores from the fourth and the eighth grades, thus addressing this issue. Although we did not have childhood IQ scores, intelligence would be reflected in scholastic testing.

Drs. Tan and Ang also raised the notion of combining neurocognitive precursors, premorbid behavioral deficits, and prodromal symptoms as an approach to screening and identifying individuals at risk of developing schizophrenia. While such an approach may be theoretically attractive, prepsychotic identification of at-risk individuals in the general population remains a daunting task, given the 1% prevalence of schizophrenia and the nonspecificity of these neurocognitive and behavioral precursors (1).

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Medication Adherence Studies in Schizophrenia

TO THE EDITOR: Annette Zygmunt, Ph.D., and colleagues (1) attempted to provide "a comprehensive summary of interventions that have sought to improve adherence to antipsychotic medication in patients with schizophrenia" (p. 1653). Unfortunately, the authors included studies in which medication adherence was neither a study objective nor an experimental variable, thus rendering suspect their conclusions about an intervention's efficacy. Since references to the literature were extensive, my group's studies of personal therapy will serve as examples (2). Medication compliance was neither a primary *nor* a secondary outcome in these studies.

Dr. Zygmunt et al. criticized personal therapy for being "no more effective than usual care in reducing medication nonadherence" (p. 1655) even though treatment was "extended" to 3 years. Ignored was the fact that strategies designed to improve medication compliance were provided to subjects in each treatment group in both trials. All patients also received psychoeducation, case management, and supportive psychotherapy services that were felt to enhance compliance further. The techniques that differed by treatment condition were the personal therapy practice principles designed to manage the effects of stress. Personal therapy was shown to have a positive effect on relapse among patients who lived with their families and significant effects on broad aspects of social adjustment (2, 3).

Although our medication and illness management approaches were fully elaborated in a recent volume regarding personal therapy (4), in the cited article, we described the effort made to enhance medication compliance for all participants (2). In order to control both extrapyramidal side effects (an important cause of noncompliance) and covert nonadherence, a majority of patients' illnesses were maintained with the minimum effective dose of depot fluphenazine or haloperidol decanoate. A smaller number of patients' illnesses were increasingly maintained with clozapine over time, with plasma levels monitored in order to ensure a therapeutic range. We provided data indicating that medication compliance was exceptionally high among all study subjects.

It is methodologically important in schizophrenia psychosocial treatment trials to minimize medication noncompliance in *both* experimental and control conditions in order to ensure that the effects of a psychosocial treatment are not the artifacts of medication. Treatment effects in personal therapy studies (as well as in the cited study of our family psychoeducational approach) were, therefore, independent prophylactic and therapeutic effects that could be causally attributed to the psychosocial interventions and not to indirect drug effects that were secondary to greater medication compliance in the experimental conditions. Dr. Zygmunt et al. inappropriately fault the efficacy of our own and other psychosocial treatments through contrasts with interventions (e.g., compliance therapy) that were designed specifically to enhance medication adherence among patients who were presumed to be at high risk for noncompliance. Comparing the primary outcome of one intervention to a secondary (or lower) outcome of another intervention is a highly questionable and potentially misleading method.

A formidable issue facing the mental health community is the reluctance to implement psychosocial interventions for schizophrenia that have been shown to forestall relapse and improve adjustment. An inaccurate portrayal of the aims and outcomes of broadly efficacious psychosocial interventions unfairly compromises the case for implementation and, in turn, the potential care of patients.

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TO THE EDITOR: Dr. Zygmunt and co-workers concluded that psychoeducation and family interventions without accompanying behavioral components and supportive services are not likely to improve medication adherence. If one seriously wishes to evaluate an intervention such as psychoeducation, one should not only carry out a review but also follow quantitative meta-analytic procedures. At a minimum, one should discuss published meta-analyses that document that these interventions can improve compliance and reduce readmission rates (1–3). Results of reviews or meta-analyses regarding psychoeducation naturally strongly depend on the definition of "psychoeducation" and, therefore, on the kind of studies included.

According to a generally recognized definition, psychoeducation does not merely mean doctors imparting information about medication. It is also necessary for therapists and participants to work together closely on an illness concept, which then creates a basis for compliant behavior. In group discussions, patients' needs and doubts are addressed. They should be in a position to make an informed decision themselves on their treatment.

Thus, we were able to show in a randomized trial involving 236 schizophrenia patients (4) that a relatively brief intervention of eight psychoeducational sessions with systematic family involvement in simultaneous groups (but without explicit behavioral components) can improve compliance and reduce rehospitalizations of schizophrenia patients significantly.

We think that empowering patients contributes considerably to the success of psychoeducation. This fact is emphasized also by some studies cited by Dr. Zygmunt et al. and is, most important, one of the first results of a concept of integrating patients in medical decisions ("shared decision making") (5). Here patients should be optimally informed that they can make evidence-based treatment choices with their doctors. The implementation of this concept in psychiatry might improve treatment adherence through improved patient involvement.

Since no data on the efficacy of this concept in schizophrenia treatment are yet available, we are currently preparing a study in which patients are involved in important treatment decisions to examine the effect of a cooperative decision on treatment adherence. Further evaluations should therefore take into account the degree to which patients are involved in therapeutic decisions.

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Dr. Boyer and Colleagues Reply

TO THE EDITOR: We share with Mr. Hogarty a concern that evidence-based psychosocial interventions have not been widely implemented, despite success in improving adjustment and preventing relapse. Our review of psychosocial interventions for enhancing medication adherence in the treatment of schizophrenia was to improve management of care. We concluded that no single strategy yielded impressive results, although targeted programs using cognitive techniques that specifically targeted patients' attitudes held much promise.

In our review, we noted that high rates of medication adherence were common in efficacy studies and, hence, that "this requirement may make it difficult to detect an increase in adherence" (p. 1661). Mr. Hogarty reinforces this point in his efforts to maximize medication adherence across groups to assess the effects of personal therapy and thus questions whether this therapy would additionally improve medication adherence. While ceiling effects limit opportunities to achieve group differences, we would like to inquire whether the interventions studied yield additional benefits for adherence. Efficacy studies are important, but a large gap remains between efficacy studies under controlled conditions and effectiveness studies in practice, where multifaceted intervention strategies must be evaluated against usual care. The literature also makes an increasingly compelling case that in achieving specifically desired outcomes, such as medication adherence or employment, targeted efforts are more effective than more diffuse ones (1). Psychoeducational efforts might usefully incorporate specific interventions directed at medication adherence. This was, in fact, what Mr. Hogarty and his colleagues did across conditions to optimize adherence (Hogarty et al., 1997).

We are grateful to Dr. Hamann and his colleagues for directing us to the eight-session psychoeducational intervention study recently reported in the German literature (Basan et al., 2000). Appropriately applied quantitative meta-analytic pro-

cedures can yield information not readily apparent from a structured literature review. At the time of our review, the literature was not sufficiently developed to support a formal meta-analysis.

We share with Dr. Hamann and co-workers an interest in studying patient involvement in clinical decision making. Educating patients to become more actively engaged in their care has been demonstrated to improve outcomes in chronic diseases (2) and may prove valuable in the care of schizophrenia as well.

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Confidentiality and the Duty to Warn of Possible Harm

TO THE EDITOR: Paul S. Appelbaum, M.D., has written extensively on privacy and confidentiality, but his recent review (1), although characteristically thoughtful and generally comprehensive, does not adequately discuss the increasing pressure on psychiatrists to report behavior that may be harmful to others. The *Tarasoff* decisions, establishing a duty to warn or to protect in other ways, initially were controversial because of concern that patients' trust would be eroded, causing them to avoid treatment or to withhold important information (2). In retrospect, this concern may have been excessive, as patients, in general, seem not to have felt betrayed by the loss of privacy in these extreme situations and the *Tarasoff* doctrine has become widely accepted (3). However, even if excessive, the concern was important, and now the pressure to report potentially harmful behavior goes far beyond the *Tarasoff* decisions' "imminent danger to identifiable persons" to encompass modest risks to larger groups. My co-authors and I (4) discussed a substance-abusing bus driver, arguing that the facts of that particular case, including the driver's weekday abstinence and his determination not to risk losing his job by failing a random drug test, justified not reporting his abuse. I have been impressed with the extent of disagreement with my conclusion, mainly in conversation, but also in print (5). Understandably, we are in a new era of heightened concern about protecting public safety. In this environment, psychiatrists, without being slavishly rule-bound, must remain sensitive to the importance of maintaining their patients' trust. Protecting confidentiality, except in extreme situations, fulfills our obligation to patients, while further erosion of confidentiality and the consequent compromise of effective treatment are likely to harm both our patients and the public at large.

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Dr. Appelbaum Replies

TO THE EDITOR: Dr. Leeman is correct to point to continuing "pressure on psychiatrists to report behavior that may be harmful to others." Sometimes that pressure has been manifest in statutes defining situations in which physicians and others must report various forms of abuse (e.g., child abuse, elder abuse, abuse of disabled persons). Other times, it has been the courts that have expanded obligations for psychiatrists to protect potential victims, as in the group of cases that derive from the California Supreme Court's decision in *Tarasoff*.

It is worth noting, however, that the evolution of psychiatrists' duties to prevent harm to third parties has not been unidirectional. Courts have often shied away from adopting more broadly framed duties, and legislatures in many states, by creating statutorily defined obligations, have restricted the circumstances in which such duties may apply. Evidence suggests that even before *Tarasoff*, psychiatrists saw themselves as having an obligation to prevent harm by their patients, when that was possible. And, as Dr. Leeman notes, both the profession and our patients seem to have acclimated to rules requiring psychiatrists and other mental health professionals to act when a substantial risk of harm exists (1).

Indeed, the case that Dr. Leeman previously reported of a substance-abusing school bus driver demonstrates that the rules we live with, in general, are both flexible and appropriate. The decision not to breach confidentiality in that case was reasonable not, as the authors suggested, because any victims of the driver would be unidentifiable in advance. Rather, the clinical evidence suggested that the patient, who avoided substance abuse on workdays and seemed highly motivated to retain his job, did not appear to present a sufficiently substantial risk to warrant reporting or other action. Based on existing legal rules, this is an entirely defensible decision.

Although the duty to report and protect potential victims of our patients can present difficult dilemmas in a small number of cases, the major threats to patients' privacy these days, as I suggested in my article, derive from efforts such as those in the current federal Health Insurance Portability and Accountability Act regulations to facilitate access to all patients' medical information for non-treatment-related purposes.

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PTSD, Acute Stress Disorder, and DSM-V

TO THE EDITOR: For a psychiatrist unfamiliar with the specific criteria for posttraumatic stress disorder (PTSD) and acute stress disorder, there were two recent articles by Ruth A. Lanius, M.D., Ph.D., et al. (1) and by Chris R. Brewin, Ph.D., et al. (2) that were extremely enlightening. The first group reported that a husband and wife who experienced the same trauma had different emotional and physiological responses to it. They were seen and assessed 4 weeks after the trauma. Both met criteria for acute stress disorder and PTSD. The wife had a high score on the Peritraumatic Dissociative Experiences Scale, but both had low scores on the Dissociative Experiences Scale. They also had different responses to script-driven traumatic imagery, as measured by T_4 functional magnetic resonance imaging, heart rate, and self-reported measures.

The second article compared the diagnostic overlap between acute stress disorder and PTSD in victims of violent crimes. Ignoring the criterion for acute stress disorder that requires it to be of only 1 month's duration, they found that 19% of the victims met the criteria for acute stress disorder and 21% for PTSD, which prominently overlapped. Both predicted an outcome of PTSD at 6 months. Could it be that in the first article the husband had typical PTSD and the wife had typical acute stress disorder (also with PTSD)? The husband did well with exposure-based treatment, but the wife did not and still had PTSD after 6 months. It could be, as Brewin et al. (2) stated, that peritraumatic dissociation is a psychological process that impedes the processing of information during the trauma. Perhaps it requires a different treatment. I do not know what the preferred treatment is for acute stress disorder.

I believe that these two articles highlight a direction for future research in this area by emphasizing the likeness and differences of these two disorders, their different pathophysiologies, and their different responses to treatment. I am not sure how the treatments relate to the treatment currently being tested for another stress-related condition, complicated bereavement.

Certainly, with such similarities, it would be imperative for the committee working on DSM-V that deals with this category to consider the overlap of these two disorders and for those who do research in this area to consider them when explaining research findings. Where, for instance, do the animal models for response to stress best fit? Are these the same reaction with different gender responses, as the first article might imply? Since both conditions usually occur immediately after a stressor, maybe the word "acute" and the 1-month duration should be dropped from the criteria for acute stress disorder.

I thank both groups of authors for their interesting articles. The first article was provocative, and the second was informative because it further quantified the criteria for the two conditions.

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Drs. Lanius and Hooper Reply

TO THE EDITOR: Our response to Dr. Clayton's letter is organized around three ideas: the limitations of diagnostic constructs, individual differences, and functional significance. Rather than seeing our subjects as having typical cases of acute stress disorder or PTSD, we emphasize that these diagnostic constructs do not adequately address the individual differences they exhibited, both subjectively and biologically, nor the functional significance of their responses.

Dissociation is used to describe a diversity of peritraumatic and posttraumatic phenomena, including emotional numbing, freezing, depersonalization, and amnesia. There are likely significant individual differences in dissociative posttraumatic symptoms among those with PTSD, and the biological bases of these phenomena are not well understood.

Indeed, the woman in our report exhibited predominantly numbing and freezing dissociative symptoms during the trauma, during the immediate aftermath, and while reliving it during script-driven imagery. Her functional magnetic resonance imaging findings were different from those we found in a study of dissociative responses to script-driven imagery in subjects with chronic PTSD who had high scores on the Dissociative Experiences Scale and significant depersonalization symptoms (1).

Individual differences are not unique to dissociative phenomena in PTSD. Blood-oxygen-level-dependent activations exhibited by the husband, who did not dissociate but described arousal and had a dramatically increased heart rate, were different from those of chronic "hyperaroused" PTSD subjects in our previous study (2) in two key structures: the anterior cingulate cortex and the thalamus.

The issue of functional significance may shed light on these issues. The wife's peritraumatic and later relived dissociative response involved feeling not only emotionally numb but, as she put it, "I could hardly move because I was completely frozen." The functional significance of a state of emotional numbness and subjectively experienced paralysis is quite different from that of a dissociated state involving significant depersonalization and an "auto-pilot" active escape mode. It should not be surprising that her brain activation pattern was different from that of the subjects with chronic PTSD with significant depersonalization symptoms. Similarly, the husband's hyperaroused state involved intensive and deliberative planning and escape cognitions, and his brain activations appeared consistent with those functionally significant activities. Of interest, studies in animals suggest that the heart rate decreases when partially restrained rats are exposed to conditioned fear stimuli (3) but increases in unrestrained rats (4).

Diagnostic categories are necessary, as are studies on relationships between the diagnostic categories of acute stress disorder and PTSD and whether these should be modified, retained, or combined (Brewin et al., 2003; reference 5). However, work on individual differences and case reports that illuminate the functional significance of specific symptomatic

responses and their biological bases also advance our understanding of posttraumatic symptoms. Such work illustrates the heterogeneity of responses in PTSD and supports the notion of Foa and colleagues (6) that different PTSD symptoms, such as intense hyperarousal or numbing, may represent distinct pathological processes. Grouping PTSD subjects with different symptom patterns within the same diagnostic category can hinder our understanding of posttraumatic psychopathology. The heterogeneity of responses in PTSD may therefore shed light on the complexities of diagnosing and treating acute and enduring posttraumatic syndromes. We thank Dr. Clayton for raising important questions that gave us an opportunity to address these issues further.

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Dr. Brewin and Colleagues Reply

TO THE EDITOR: We are pleased that Dr. Clayton raised the interesting issue of how best to interpret our finding that acute stress disorder and PTSD can be commonly diagnosed simultaneously, provided that the time criterion requiring PTSD symptoms to have been present for 1 month is ignored. This observation was illustrated by the patients described by Dr. Lanius et al. Our own conclusions are somewhat different from those of Dr. Clayton. In our opinion, our data make it hard to sustain the position that acute stress disorder and PTSD are two distinct disorders. We prefer to think that there is only one disorder but that specific processes may be present or absent and have a corresponding impact on pathophysiology. There are now several studies that implicate peritraumatic dissociation in explaining the variability in the psychophysiological reactions of patients with PTSD and suggest that such dissociation may reflect a freezing response as opposed to a fight-or-flight response (1). There are a number of reasons why one person responds to exposure therapy and another does not. For example, negative emotions, such as shame (2), and negative beliefs about the trauma or about subsequent symptoms (such as dissociation) have been shown to impede recovery. Our guess is that the payback will be greater from understanding these processes than from further refining our diagnoses.

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