We do agree with Dr Carroll that the definition of hypothalamic-pituitary-adrenal axis “dysfunction” is open to discussion. While the reported differences in cortisol concentration and cortisol concentration change after dexamethasone administration might seem “physiologically minor” or “trivial,” they are correlated with significant differences in gene expression in peripheral blood cells and the affected genes often carry glucocorticoid response elements. We thus observe biological consequences on the gene expression level in peripheral blood of these “trivial” differences. Furthermore, such “minor” differences as recorded by a one-time measure of plasma cortisol levels may have biological consequences on immune and brain function, so we feel that the term trivial should only be used once all biological consequences are taken into account and should not restrict itself to the plasma levels alone. In addition, our data also suggest that it is important to carefully select the comparison group. Individuals with different functional genetic polymorphisms seem to differ in the set point of their stress hormone system parameters, and disease-related differences may only be apparent within a specific genotype group.

Based on our responses, we do not feel that Dr Carroll’s concerns challenge the conclusions of the article. Thank you for your consideration.

Elisabeth Binder, MD, PhD
Divya Mehta, PhD
Kerry Ressler, MD, PhD
Florian Holsboer, MD, PhD

Author Affiliations: Max-Planck Institute of Psychiatry, Munich, Germany (Drs Binder, Mehta, and Holsboer); Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine (Drs Binder and Ressler), and Yerkes National Primate Research Center (Dr Ressler), Atlanta, Georgia; and Howard Hughes Medical Institute, Chevy Chase, Maryland (Dr Ressler)

Correspondence: Dr Binder, Max Planck Institute of Psychiatry, Kraepelinstrasse 2, Munich 80804, Germany (binder@mpipsykl.mpg.de).

Financial Disclosure: Drs Binder and Holsboer have filed patent applications as inventors of “Means and Methods for Diagnosing Predisposition for Treatment Emergent Suicidal Ideation (TESI)” (European application 08016477.5; international application PCT/EP2009/061575) and “FKBP5: A Novel Target for Antidepressant Therapy” (international publication WO 2005/054500). Dr Holsboer is a founder and shareholder of Afectis Pharmaceuticals. Within the last 3 years, Dr Ressler has received research funding support from Lundbeck, and he has an unrelated role as cofounder of Extinction Pharmaceuticals for development of N-methyl-D-aspartate–based therapeutics. Dr Binder has current grant support from PharmaNeuroBoost.

Additional Information: This letter was written on behalf of all authors of “Using Polymorphisms in FKB5 to Define Biologically Distinct Subtypes of Posttraumatic Stress Disorder: Evidence From Endocrine and Gene Expression Studies.”

8. Wiedemann K, Holsboer F. Plasma dexamethasone kinetics during the DST after oral and intravenous administration of the test drug. Biol Psychiatry. 1987;22(11):1340-1348

Errors in Table and Results. In the Original Article by Dick et al titled “Role of GABRA2 in Trajectories of Externalizing Behavior Across Development and Evidence of Moderation by Parental Monitoring,” published in the June 2009 issue of the Archives (2009;66[6]:649-657), Tables 3 and 4 contained errors in the single-nucleotide polymorphism labels, P values, odds ratios, and 95% confidence intervals. In the “Results” section, all references to the minor allele actually refer to the major allele, and all findings regarding rs497068 actually correspond to rs279826. This article was corrected online.