ELSEVIER

LETTER TO THE EDITOR

Does Rapid Tryptophan Depletion Induce Depressive Relapse?☆

Moore et al offer an excellent, comprehensive scientific review of tryptophan depletion experiments (Moore et al. 2000). A key issue examined in the article is the "reported ability [of rapid tryptophan depletion] to induce depressive relapse in euthymic patients." The appropriateness of defining transient depressive symptom exacerbation as a "depressive relapse" is a matter of scientific, clinical, and ethical significance. The description of tryptophan depletion as provoking "relapse" in euthymic patients misleadingly suggests that these experiments make patients clinically depressed for the sake of scientific investigation, thus provoking unwarranted ethical criticism.

The authors note that "depressive relapse" has been defined variously by different investigators, and they endorse the "most restrictive" definition adopted by Delgado and his colleagues: "an increase in pre-challenge HDRS by at least 50% and >17." The authors do not provide systematic data on the duration of provoked symptom worsening. Delgado et al. described tryptophan depletion in 46 patients in remission following antidepressant treatment, of whom 24 experienced "depressive relapse." (Delgado et al. 1991) They observed that "All of these patients returned to their clinically remitted state within 24 to 48 hours after the TRP-depleting amino acid drink."

We contend that such transient symptom exacerbation does not amount to depressive relapse. Depressive relapse constitutes a serious and persisting emergence of symptoms that warrants pharmacological intervention. (Frank et al. 1991) Symptom exacerbation lasting from a few hours to up to two days is clinically and ethically significant in view of the distress that it may cause. (Miller and Rosenstein 1997) But these results do not support a claim that tryptophan depletion experiments induce clinically significant relapse in some patient volunteers. The definition of "depressive relapse" employed in the tryptophan depletion and other challenge paradigms is problematic because it focuses solely on symptom severity and not on duration. More careful characterization of symptom provocation associated with psychiatric challenge studies promotes both scientific and ethical accuracy.

Franklin G. Miller, Ph.D.
Donald L. Rosenstein, M.D.
National Institutes of Health
Bethesda, MD

REFERENCES

Moore P, Landolt H-P, Seifritz E, Clark C, Bhatti T, Kelsoe J, Rapaport M, Gillin JC (2000): Clinical and physiological consequences of rapid tryptophan depletion. Neuropsychopharmacology 23:601–622

Delgado PL, Price LH, Miller HL, Salomon RM, Licinio J, Krystal JH, Heninger GR, Charney DS (1991): Rapid serotonin depletion as a provocative challenge test for patients with major depression: relevance to antidepressant action and the neurobiology of depression. Psychopharmacology Bulletin 27:321–330

Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, Rush AJ, Weissman MW (1991): Conceptualization and rationale for consensus definitions of terms in major depressive disorder. Archives of General Psychiatry 48:851–855

Miller FG, Rosenstein DL (1997): Psychiatric symptom-provoking studies: an ethical appraisal. Biological Psychiatry 42:403–409

☆Refers to PII S0893-133X(00)00161-5

The opinions expressed are those of the authors and do not necessarily reflect the position or policy of the National Institutes of Health, the Public Health Service, or the Department of Health and Human Services.

Published by Elsevier Science Inc.
655 Avenue of the Americas, New York, NY 10010

0893-133X/01/$–see front matter
PII S0893-133X(01)00260-3