The first factor is an important methodological one. If patients had one or more brief hypomanias and then progressed to having full duration or more severe episodes, only the latter, most severe episode was counted. Thus, the apparent decrease in minor or subthreshold switches appears to be related to the fact that more patients receiving venlafaxine progressed to full duration hypomanias or manias relative to the patients given the other drugs.

Also consistent with this interpretation are the findings, based on this same cohort, that were analyzed using conventional cross-sectional measures of manic severity as reported in a companion article (1). If one used a two-point or greater increase in the Clinical Global Impression Scale for Bipolar Disorder mania severity rating as indicating a clinically meaningful switch, this criterion occurred in more patients receiving venlafaxine ($p<0.01$). Similarly, if one used the criterion of a Young Mania Rating Scale score of >13 as an indication of clinically meaningful hypomania or mania, this also occurred more frequently with venlafaxine ($p=0.05$), especially in rapid cyclers. Moreover, Vieta and colleagues (2) also found higher switch rates with venlafaxine than paroxetine in a randomized open study.

Thus, the graded Young Mania Rating Scale and Clinical Global Impression Scale for Bipolar Disorder manic severity ratings used by Post and colleagues (1) and the methodological clarification that only the most severe form of manic switch observed was counted suggest that there is an increased proclivity for full switches with venlafaxine relative to the other two drugs (particularly bupropion). On the basis of both analyses, we would conclude that greater caution is warranted (particularly in those patients with a prior history of four or more episodes in the year prior to study entry) in the use of antidepressant adjunctive treatment with venlafaxine than sertraline or bupropion in the treatment of depressed patients with bipolar disorder who are already receiving a mood stabilizer.

References

1. Post RM, Altshuler LL, Leverich GS: Higher switch rates on venlafaxine than bupropion or sertraline in bipolar depression. Br J Psychiatry (in press)
2. Vieta E, Martinez-Aran A, Goikolea JM, Torrent C, Colom F, Benabarre A, Reinares M: A randomized trial comparing paroxetine and venlafaxine in the treatment of bipolar depressed patients taking mood stabilizers. J Clin Psychiatry 2002; 63:508–512

GABRIELE S. LEVERICH, M.S.W., L.C.S.W.C.
Bethesda, Md.

Reduced Hippocampal and Amygdalar Volume in Dissociative Identity Disorder: Not Such Clear Evidence

TO THE EDITOR: As experimental psychologists trained in research methodology, we read the article by Eric Vermetten, M.D., Ph.D., and colleagues (1) with mixed feelings. The authors employed magnetic resonance imaging (MRI) to measure the volumes of the hippocampus and amygdala in 15 female patients with dissociative identity disorder and 23 female nonpsychiatric women. Dr. Vermetten and colleagues concluded from their data that, relative to comparison subjects, patients with dissociative identity disorder had smaller hippocampal and amygdalar volumes. They admit that their study suffers from a number of shortcomings. Most important, the patients with dissociative identity disorder were significantly older than the comparison subjects. Although group differences in hippocampal and amygdalar volumes disappeared when the authors statistically controlled for age, they try to convince the reader that their results are nonetheless valid. They argue that there is generally no age-related reduction in hippocampal and amygdalar volumes in healthy women aged 20–50. This point is reiterated in an editorial by David Spiegel, M.D. (2, p. 566), who stated that the article by Dr. Vermetten and colleagues offers "clear evidence of smaller hippocampal and amygdalar volume among those with dissociative disorders" (2). Unfortunately for Dr. Vermetten and colleagues as well as Dr. Spiegel, there have been reports that this population also exhibits significant, albeit moderate, hippocampal volume decreases in a 5-year follow-up design (3). In relation to this, there is good evidence that suffering from a major psychiatric disorder may lead to accelerated aging in middle-aged people (4, 5). Therefore, MRIs of healthy, younger individuals do not constitute the ideal control condition for those of patients with dissociative identity disorder. It is with these considerations in mind that we fundamentally disagree with Dr. Spiegel when he claims that the study by Dr. Vermetten and colleagues offers "clear evidence." It does not.

References

1. Vermetten E, Schmahl C, Lindner S, Loewenstein RJ, Bremner JD: Hippocampal and amygdalar volumes in dissociative identity disorder. Am J Psychiatry 2006; 163:630–636
2. Spiegel D: Recognizing traumatic dissociation. Am J Psychiatry 2006; 163:566–568
3. Raz N, Rodrigue KM, Head D, Kennedy KM, Acker JD: Differential aging of the medial temporal lobe: a study of a five-year change. Neurology 2004; 62:433–438
4. Houx PJ, Vreeling FW, Jolles J: Rigorous health screening reduces age effect on memory scanning task. Brain Cogn 1991; 15:246–260
5. Rabbitt PMA, McInnes L, Diggle P, Holland F, Bent N, Abson V, Pendleton N, Horan M: The University of Manchester longitudinal study of cognition in normal healthy age, 1983 through 2003. Aging Neuropsychol Cogn 2004; 11:245–279

TOM SMEETS, MS.C.
MARKO JELICIC, PH.D.
HARALD MERCKELBACH PH.D.
Maastricht, the Netherlands

Dr. Vermetten Replies

TO THE EDITOR: We acknowledge that the design of every study is strongest when groups that are studied are matched for several dependent variables. However, we argue that the data disputed by Drs. Smeets, Jelicic, and Merckelbach are strong and valid. Hippocampal volume was 19.2% smaller and amygdalar volume was 31.6% smaller in the patients with dissociative identity disorder relative to the healthy subjects. Statistical rigor required us to control for the age difference (dissociative identity disorder patients [42.8 years] versus comparison subjects [34.6 years]). In doing so, our findings left only the right amygdalar volume significantly smaller across groups. However, we argue that the comparison data for the hippocampal and amygdalar volumes are valid without correction for this factor. Even though age-related structural alterations in the hippocampus have been identified, there are no