Response

To the Editor:

We appreciate Dr. Kramer's comments and while we agree with many of his general assertions, we feel that he has mixed up several related but distinct issues: (1) change in positive and negative symptoms with neuroleptic treatment in the acute phase of the illness (this was the question addressed in our present study) (2) the measurement of negative symptoms and their delineation from phenomena such as depression and EPS; (3) the relationship of cholinergic hyperactivity to negative symptoms and the possible role of anticholinergics in their treatment.

In our study, we *observed* that negative symptoms improved in tandem with positive symptoms. Factors such as EPS and akinetic depression did not confound this observation as baseline negative symptom ratings (from which improvement was measured) were performed when patients were drug-free for a minimum of 2 weeks and both psychotropic-naive and previously treated patients showed this same pattern of improvement. Despite the phenomenological overlap between depression and negative symptoms, recent studies (including our own, Liberzon et al 1990), indicate that these phenomena can be distinctly measured. With regard to positive symptoms, most experts consider positive and negative to be distinct symptom dimensions, which may be related at some phases of the illness. Our finding do suggest that psychotic-phasic negative symptoms may differ from deficit-enduring negative symptoms with regard to neuroleptic-responsiveness and covariance with positive symptoms, but to further infer that the former are not "true negative symptoms" would be premature (Andreasen 1990; Tandon and Greden 1990).

The implications of our findings are less clear. Several mechanisms (including concomitant reduction in dopaminergic and cholinergic activity) can be invoked to explain these findings. Thus, although these findings would be consistent with our model of concomitant increases in dopaminergic and cholinergic activity in the psychotic phase of schizophrenic illness (related to positive and negative symptoms, respectively), other explanations are plausible as well. We would like to underscore the point that the dopaminergic/cholinergic model and the implication of cholinergic hyperactivity in the production of negative symptoms are *hypotheses to be tested*, and the study suggested by Dr. Kramer might be one way to test it.

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Epstein-Barr Virus Antibodies and Severity of Depression

To the Editor:

While laboratory evidence of impaired cellular immune function has been reported in patients with affective disorders (Kronfol et al 1983, 1985; Schleifer et al 1984; Syvalahti et al 1985; Albrecht et al 1985; Irwin and Gillin 1987), this has not been linked to an increased risk of clinical infection in these patients. Antibodies reactive with Epstein-Barr Virus (EBV)-associated antigens are present in most adults, indicating endemic latent infection with this pathogen. Elevated titers of these antibodies are seen in a variety of immunocompromised states, presumably indicating persistent active or reactivated infection as