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In Reply

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The mean alcohol intake was less than 8 units weekly.

Scanning at 0.5 T covered the entire cerebrum in contiguous 5-mm slices, which were selected to give good contrast between white matter and focal hyperintensities. Each scan was rated blindly by an experienced neuroradiologist. Two of these controls showed only one isolated white matter abnormality, four controls had two such abnormalities, and one control had more than five abnormalities. Of these seven controls, four had abnormalities in the right hemisphere and five had them in the left. Of a total of 21 such abnormalities, 13 were situated in the frontal lobe; while this partly reflects the greater emphasis given to this area, which was scanned with additional quences, it echoes the distribution noted by Dupont and colleagues. These abnormalities were all punctate foci, with clearly increased signal, rarely more than 5 mm in diameter, and obviously separate from both ventricles and sulci; they looked very similar to those noted by Dupont et al. Doubtful changes were not included.

It is often regarded as uncommon to observe such white matter changes in healthy people younger than 50 years of age, but it may be that the healthy controls most ready at hand, such as physicians and radiology technicians, have given us a biased view. People from a less privileged background may reveal a different story. Dupont et al noted that those patients with such white matter changes had lower neuropsychologic test performance results than those without such changes, and we suggest that these two variables may be significantly associated in the general population and not just in bipolar disorder.

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In Reply.—We appreciate the interest and comments of Drs Harvey, Ron, du Boulay, Murray, and Lewis regarding our recent article in the ARCHIVES.

The authors commented that the expected rate of signal hyperintensities in younger subjects is greater than 0. We agree that this is the case, and suspect that chance sampling variation resulted in a rate of hyperintensities in our control subjects that underestimated the prevalence of these abnormalities in young subjects. However, although greater, the rate reported by Harvey et al is not significantly different from the rate in our control group (Fisher's Exact Test; $P<.32$). Furthermore, we do not wish to leave readers with the impression that the finding of white matter abnormalities in a sample of bipolar patients is in itself of interest. It is the increased rate of hyperintensities in the bipolar subjects compared with controls that is intriguing. When the rate in our bipolar patients is compared with the rate in their controls, the difference is still statistically significant (χ^2, $P<.03$).

With regard to the comment by Harvey et al about the choice of controls, we are again in agreement. They state that available medical personnel would give a biased view if used as controls. For this reason, our controls were prospectively screened to be matched for age and education to our patient group.

Finally, the last point of the authors, that impaired neuropsychological performance may be associated with white matter abnormalities in the general population, is intuitively attractive. In fact, while the definitive study of concurrent magnetic resonance imaging and neuropsychological testing on normal controls has yet to be done, there are frequent reports that otherwise healthy, unimpaired individuals demonstrate these abnormalities. Nevertheless, it would not be surprising if careful neuropsychological examination of normal subjects with white matter abnormalities revealed a pattern similar to that of the bipolar subjects.

We also agree with Dr Epstein that smoking is a significant risk factor for atherosclerotic vascular disease. As noted in our article, this is a possible etiology for similar types of lesions. It is unlikely to be the sole causative factor in our bipolar patients, however, since five of the patients with lesions stated they had never smoked.

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