Letters to the Editor

LSD and Schizophrenia

To the Editor.—Vardy and Kay,[1] reporting on LSD and schizophrenia, have addressed a significant issue for those attempting to define the nature and etiology of schizophrenic illnesses. The role of LSD and other hallucinogens, dopamine, and other amines (endogenous or exogenous) in functional psychoses still remains to be clarified. There has been dispute as to whether intoxication with LSD is a good model for schizophrenic psychosis (with the predominance of opinion being that it is not), and uncertainty as to the relative role of monoaminergic pathways in schizophrenic illness. With respect to LSD (which is clearly active in serotoninergic systems[2]) and serotoninergic activity in schizophrenics, at least eight studies have suggested serotoninergic abnormalities in schizophrenia.[3-8] The conclusion reached by Vardy and Kay was that, in most respects, their patients who had LSD-induced psychosis could not be significantly differentiated from control schizophrenics.[1] There are problems with their study, however, which make interpretation difficult.

The course of illness in terms of subsequent hospitalizations for the two groups was similar during the next three to five years. However, no information was given as to whether subsequent hospitalizations represented recurrences of drug-induced psychosis in patients who did not manifest psychotic symptoms when free of drug use, or whether in fact recurrent psychotic episodes developed in those patients without further drug abuse. This would be pertinent to the question of an underlying predisposition to schizophrenia in those patients.

The incidence of parental illness requiring hospitalization was found to be essentially the same in the groups with LSD-induced psychosis and schizophrenia. The relevant issue, however, is the incidence of *schizophrenia* in the parents of subjects in these two groups. In their study, Vardy and Kay included all parents with a history of "mental illness requiring hospitalization," which would likely include a significant proportion of parents with major depressive episodes, bipolar disorder, and other conditions in addition to schizophrenia.[1] The sample was sufficiently small so that pursuit of the records of hospitalized parents might be feasible to clarify this issue. A related problem is that the incidence of schizophrenia in parents of schizophrenics was obtained from the literature rather than from the parents of the control group. Since the control group was from the same institution, was it feasible to obtain the incidence of schizophrenia from the case records of parents for a more valid comparison?

A significant study, not noted by the authors, was done using patients in a Veterans Administration Hospital,[9] and supports the conclusion by Vardy and Kay that hallucinogen abuse might precipitate chronic psychosis in the schizophrenic spectrum.[1] Due to the methodologic limitations mentioned, however, I think it is premature for the authors to have stated that the family history and subsequent course of schizophrenics and patients with LSD-induced psychosis do not differ. Further exploration is warranted.

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In Reply.—Dr Weaver has posed some thoughtful questions about our article that deserve a point by point reply.

1. Regarding the nature of the rehospitalizations of our patients who used LSD, patients' self-reports on follow-up interview, as well as their hospital records, indicated that their readmissions were not related to LSD or other hallucinogenic drugs. As a matter of fact, only two of the 21 patients in the LSD follow-up group reported that they had used LSD occasionally since their first hospitalization, but they were *not* among those who were readmitted. Some of the rehospitalized patients reported some occasional use of marijuana or alcohol, but there is no evidence that their use was related to their relapses.

2. As we have noted in our report, we could not with confidence rule out the possibility (which we suspected) that there were major depressive or bipolar illnesses among the reported cases of parental psychosis requiring hospitalization. Unfortunately, the patients' family reports on which the data were based did not include specifics on the exact diagnosis of the hospitalized parent. Furthermore, in most cases, the hospitalization of the parent occurred many years before that of the offspring and in hospitals other than our own, so that these records could not be pursued reliably.

3. To compare the incidence of parental psychosis in our LSD-using sample (n = 52) with the small number of schizophrenics in our comparison group (n = 29) would have opened the study to the strong likelihood of type II error, ie, affirming the absence of difference when indeed one may have existed.[1] This is especially true since the effect size, ie, the incidence of parental psychosis in LSD-using patients (13.5%), was also small, and only a vast difference between the two groups would have achieved statistical significance. Therefore, we chose instead to use the larger epidemiologic sample of Fowler et al,[2] which increased the statistical power and decreased the chance of bias in the direction of type II error, allowing us to conclude with greater confidence that patients with LSD-induced psychosis are not different from schizophrenics in their rates of parental psychosis.

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LSD Flashbacks

To the Editor.—I read with interest Abraham's article on "Visual Phe-