

## DOES A HISTORY OF POSTICTAL PSYCHOSIS PREDICT A POOR POSTSURGICAL SEIZURE OUTCOME?

**Postictal Psychosis in Partial Epilepsy: A Case-Control Study.** Alper K, Kuzniecky R, Carlson C, Barr WB, Vorkas CK, Patel JG, Carrelli AL, Starner K, Flom PL, Devinsky O. *Ann Neurol* 2008;63(5):602–610. **OBJECTIVE:** Divergent findings among prior studies on correlates of risk for postictal psychosis (PIP) suggest the value of a controlled study involving a relatively large number of patients. **METHODS:** The study population consisted of a consecutive series of 59 patients with partial epilepsy and a history of PIP, and 94 control patients with partial epilepsy and no history of PIP evaluated as inpatients with video-electroencephalography. The groups did not differ significantly regarding demographic features. Exact tests yielded a subset of variables and a tentative interpretation that were evaluated further utilizing principal components analysis and logistic regression. **RESULTS:** PIP was associated with extratemporal versus temporal ( $p = 0.036$ ) or undetermined ( $p = 0.001$ ) localization of seizure onset, bilateral interictal epileptiform activity ( $p = 0.017$ ), secondary generalization ( $p = 0.049$ ), and history of encephalitis ( $p = 0.018$ ). Interictal slow activity was more frequently absent in control patients ( $p = 0.045$ ). PIP was associated with family histories of psychiatric disorders ( $p = 0.007$ ) and epilepsy ( $p = 0.042$ ), which themselves were significantly intercorrelated ( $r = 0.225$ ;  $p = 0.006$ ). Age of onset or duration of epilepsy and lateralized electroencephalographic or magnetic resonance imaging asymmetries did not differ significantly between control and PIP groups. The analysis indicated four underlying domains of risk for PIP: ambiguous/extratemporal localization, family neuropsychiatric history, abnormal interictal electroencephalographic activity, and encephalitis. Each unit increase on a simple additive scale composed of 9 dichotomous independent variables multiplied the odds ratio for PIP by 1.71 (95% confidence interval, 1.36–2.15;  $p < 0.0001$ ). **INTERPRETATION:** PIP in partial epilepsy is associated with relatively broadly and bilaterally distributed epileptogenic networks, genetic determinants of psychiatric disorders and seizures, and encephalitis.

### COMMENTARY

Predictors of postsurgical outcome typically include ictal and interictal data obtained from video-EEG monitoring studies (which provide location and number of interictal and ictal foci), neuroimaging data (which reveal the presence of structural lesions, hippocampal atrophy, and other structural features), as well as taking into consideration the type of epileptic seizures (generalized tonic-clonic seizures vs complex partial seizures) the patient experiences. While psychiatric history is not typically thought of as a predictor of postsurgical seizure outcome, a history of postictal psychotic (PIP) episodes may be one of the exceptions.

Postictal psychosis corresponds to approximately 25% of psychosis associated with epilepsy. The prevalence rates of PIP episodes have been estimated to range between 6 and 10 percent (1). In patients with partial epilepsy who have undergone a video-EEG, the yearly incidence of postictal psychosis was reported to be 6.4% (2). Several case series have identified the following clinical characteristics of PIP episodes: 1)

A symptom-free period, ranging from 12 to 120 hours, occurs between the time of the last seizure and the onset of the psychiatric symptoms. 2) Insomnia and/or agitation is one of the initial symptoms; it precedes the onset of psychotic symptoms by 8 to 24 hours. 3) Psychotic episodes of relatively short duration (i.e., hours-to-days, rarely weeks) appear and consist of affect-laden delusions, hallucinations, agitation, and thought disorder. 4) The onset of postictal psychosis follows a 10-year history of a pharmacoresistant seizure disorder. 5) With administration of a low-dose antipsychotic medication or occasionally benzodiazepines, a prompt symptom remission transpires. 6) Finally, secondarily generalized tonic-clonic seizures occur, often in clusters and with bilateral interictal and ictal foci (2–7). Accordingly, a study that involved 18 consecutive patients with partial seizure disorders and postictal psychosis found that a history of PIP episodes was predictive of bilateral ictal foci with an 89% certainty compared with the 18 controls (7). In the study by Alper et al., patients with postictal psychosis were significantly more likely than controls to have extratemporal or poorly localized ictal foci, generalized tonic-clonic seizures, as well as a history of encephalitis. Not surprisingly, the epilepsy-related variables associated with postictal psychosis in this study and in those

cited here have been linked with poor postsurgical seizure outcomes.

While it may be reasonable to assume from these data that a history of PIP episodes might exclude patients from an epilepsy surgery *evaluation*, there are compelling reasons to do the opposite. While PIP episodes are of short duration and respond to low doses of antipsychotic medication, the long-term prognosis for these patients may not be all that favorable, as postictal psychosis can evolve into interictal psychotic episodes. For example, in a study of 18 consecutive patients with partial epilepsy and PIP episodes, 7 (39%) individuals went on to develop interictal psychotic episodes. In contrast, only 1 of the 18 control patients with partial epilepsy and no history of PIP episodes developed interictal psychotic episodes (8). Other authors have replicated these findings (9). Thus, in recommending epilepsy surgery for patients with postictal psychosis consideration must be given not only to the desire to achieve seizure freedom but also to the need to prevent the development of an interictal psychotic episode. However, not all patients have bilateral or extratemporal ictal foci, thus some individuals with PIP episodes may be good surgical candidates. Even for patients with bilateral, independent ictal foci, palliative surgery can be considered, if the mesial temporal sclerosis is unilateral and the majority of seizures (>80% of all recorded typical seizures) originate from the atrophic hippocampal formation. In addition, the neuropsychological and intracarotid sodium amytal test data would need to suggest that the patient is at low risk of suffering significant postsurgical memory deficits. Patients that meet these criteria have up to 50% probability of achieving a seizure-free state. However, a cautionary note is in order: when patients with PIP episodes are being evaluated for epilepsy surgery, they must be advised that the procedure will put them at an increased risk of postsurgical manic and depressive episodes, which are likely to occur during the first 3 months after surgery (10).

Finally, given the data presented here, several practical steps can be taken to evaluate patients with a history of postictal psychosis or suspected to be at risk for postsurgical PIP episodes. In order to identify or rule out the presence of bilateral independent ictal foci, a relatively large number of epileptic seizures (>5 seizures) need to be recorded during the video-EEG. Prophylactic treatment with low-dose atypical antipsychotic drugs (e.g., risperidone or quetiapine) may be necessary to minimize the risk of developing postictal psychosis following the occurrence of the large number of seizures, particularly if they are generalized tonic-clonic (2). Regardless, patients, who have bilateral ictal foci identified by video-EEG, must be closely observed for the development of PIP episodes, particularly if there

is a family history of psychiatric disorders. Indeed, in the study by Alper and colleagues, having a psychiatric family history was found to be an independent risk factor for developing PIP episodes (OR: 2.6, 95% CI: 1.21–5.65). Yet, since PIP episodes can appear several days after the last seizure, often occurring after the individual has been discharged, patients and their families must be instructed to identify the common initial symptoms, as previously delineated (e.g., insomnia, agitation). If these symptoms are identified, a low dose of an atypical antipsychotic drug can be administered to abort the full-blown psychotic episode.

In conclusion, a history of postictal psychosis (or the development of PIP episodes in the course of a video-EEG) should serve a red flag to the presence of bilateral independent ictal foci and/or diffuse brain damage—both of which have been associated with a poor postsurgical seizure outcome. Yet, this red flag should not be interpreted as a categorical reason to exclude these patients from consideration for an *evaluation* of epilepsy surgery.

by Andres M. Kanner, MD

## References

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