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The Reply:

We agree with Friedman that quetiapine and risperidone are not comparable in terms of their potential to worsen motor features of parkinsonism. In Table 1 of our publication,[1] we stated that quetiapine has a "low" potential and risperidone has a "medium to high" potential to cause extrapyramidal side effects in the 3 parkinsonian conditions we discussed. This difference also is specified within the text. Specifically in regard to psychosis associated with Parkinson's disease, we noted, "Several open-label studies reported that quetiapine possesses modest efficacy against psychosis with few motor side effects in a heterogenous group of patients with psychosis and parkinsonism" and "Although risperidone can improve psychosis associated with Parkinson's disease, information about its side effects is limited and mixed." Both these statements are substantiated in the literature. Our statement about the potential of risperidone to cause motor side effects is similar to that made by Fernandez et al[2] in their publication, of which Friedman was a co-author. They stated, "Although some studies have reported risperidone to be well tolerated in patients with Parkinson's disease, other studies have shown that many patients are unable to tolerate the drug because of the deterioration of motor function."

Antipsychotic drug treatment-associated worsening of parkinsonism derives from the receptor-binding profile of these medications, their dose, and the nature and extent of the preexisting parkinsonism. Risperidone, as well as quetiapine and olanzapine, can cause extrapyramidal side effects comparable to those of conventional antipsychotic drugs when used at higher doses in the elderly.[3] Leopold[4] reported favorable results with risperidone, commenting that motor side effects of risperidone were more prominent in previous studies that included patients with advanced Parkinson's disease or when risperidone was used at high doses. In a double-blind study on 10 subjects, Ellis et al[5] found risperidone (0.5-1.5 mg/d) comparable to clozapine and suggested, "Risperidone may be a reasonable alternative to clozapine in the treatment of psychosis in subjects with PD." In regard to the utility of other atypical antipsychotics, we noted[1] that routine use of olanzapine is not recommended, data on aripiprazole are not encouraging, and data on ziprasidone and paliperidone are lacking. After taking these observations into account, we believe risperidone at low dosages of 0.25 to 1 mg per day may be a reasonable second-line option for psychosis associated with early Parkinson's disease (without dementia).

We appreciate Friedman pointing out that in a study we cited regarding the use of clozapine to treat Parkinson's disease psychosis, a subanalysis of the data did not find differences in efficacy between demented and non-demented subjects with Parkinson's disease.

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