with duration of positive symptoms. This work, as well as the phosphorus work by our team (Jensen *et al*, 2000, 2002), suggests a gradual neurodegenerative process in the anterior cingulate in schizophrenia, possibly initiated by an early neurodevelopmental anomaly involving basal ganglia–thalamocortical neuronal circuits or the structures which regulate these circuits. As Dr Rands points out, memantine would partially block the NMDA receptors preventing excitotoxic damage in the anterior cingulate and connected structures, thus slowing the progression of symptoms. However, there are other considerations. There is evidence that excitotoxicity is linked to non-NMDA receptors (Tsai & Coyle, 2002) which may not be affected by this approach. Furthermore, another NMDA-blocker, phencyclidine, can actually cause a paradoxical increase in glutamate activity which could aggravate the condition.

In summary, we agree that treatment options for schizophrenia should begin to focus more on this neuroprotective strategy. Although current medications may alleviate positive symptoms, they are relatively ineffective for negative symptoms and are often inadequate in preventing the psychosocial deterioration seen in chronic schizophrenia. Treatment with memantine could theoretically slow the progression of negative symptoms when administered to patients in the early stages of schizophrenia but the overall effects of these drugs are difficult to predict and it is our view that some caution is indicated in planning long-term trials of these medications in people with schizophrenia.

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Testing for diabetes

Taylor *et al* (2004) report on the differences in testing for diabetes among 606 patients receiving antipsychotics, observing that patients receiving atypical antipsychotics were more likely to have been tested than those receiving older agents. Moreover, this appeared to be significant specifically for clozapine, olanzapine, and antipsychotic polypharmacy.

It is noteworthy that very similar results were found by our group when examining hospitalised patients in New York State (Citrome *et al*, 2003, 2004). Among 1154 patients in 2000–2002 with no known prior history of receiving antidiabetic medications, those receiving clozapine, olanzapine, or more than one atypical antipsychotic had a significantly higher frequency of blood glucose testing than those receiving only typical antipsychotics (Citrome *et al*, 2004). Moreover, those receiving risperidone had a frequency of testing similar to those receiving only older agents, resulting in the conclusion that there are clear differences in surveillance for diabetes mellitus among even the newer agents.

Investigators performing pharmacoepidemiological studies examining the risk of association between antipsychotics and diabetes mellitus need to be mindful of this surveillance bias.

Declaration of interest

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Taylor *et al* (2004) found very low rates of monitoring for diabetes in their study population. Less than 50% were tested, and the testing rates varied with the antipsychotic prescribed.

So why is this the case? This probably reflects the lack of a clear consensus in this area. There is currently no consistent direction for doctors regarding the need for monitoring for diabetes. The conflicting evidence in the literature is abundant. For example, the *British National Formulary* is probably the most widely used reference for prescribers in the UK. The current edition makes no mention of blood sugar abnormalities with typical antipsychotics, quetiapine and risperidone. Concerns are mainly highlighted with olanzapine and clozapine. This is despite studies showing increased risks with typical and atypical antipsychotics. Furthermore, the recent Maudsley Guidelines give some suggestions of the type and frequency of tests, focus mainly on olanzapine and clozapine but contradict the *British National Formulary* in suggesting testing for all antipsychotics.

So is testing important? Evidence is mounting of an association between schizophrenia and diabetes. Ryan & Thakore (2002) give schizophrenia as an independent risk factor for diabetes even in antipsychotic-naïve patients. The PORT study (Dixon *et al*, 2000) gives a prevalence of 15% in this population compared with 3% in the general population (Bennett *et al*, 1995). Several studies suggest an even higher risk of diabetes in those prescribed atypical antipsychotics (Bushe & Leonard, 2004). Therefore, it appears that people with schizophrenia are a high-risk group for developing diabetes and its potential consequences.

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