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We agree that it is important to establish whether antipsychotics are superior to other sedative drugs for the treatment of acute psychotic symptoms, and hence appreciate the review by Sifakis et al. (2019). We would like to correct a misperception of our work, however (Moncrieff & Cohen, 2005). We did not suggest that antipsychotics are merely active placebos, nor that they are identical in their effects to other sedatives. In line with Sifakis et al. (2019), we pointed out that some trials found that antipsychotics were superior to barbiturates for the treatment of schizophrenia, but that current evidence has not established that they are different from benzodiazepines in their effectiveness. What we also suggested was that there is no evidence that antipsychotics, or any other drug prescribed for a mental disorder, produce their therapeutic effects by reversing an underlying brain-based abnormality. The effects of antipsychotics are more likely to be the result of the alterations to normal brain functioning that they produce. These alterations result in particular psychological and behavioural changes that are sometimes subtly and sometimes obviously different from those produced by other sedatives, and may be more effective in suppressing psychotic symptoms. Unlike barbiturate-like sedatives, antipsychotics produce a state of emotional indifference and reduced initiative and motivation alongside varying degrees of sedation and mental slowing, effects which can make psychotic symptoms less intense and intrusive. Indeed, this was the way that antipsychotics were thought to work by the pioneers of modern psychopharmacology in the 1950s and 1960s, who commented on the ‘psychic indifference’ (Anton-Stephens, 1954), ‘pathological tranquillity of mind’ (Winkelman, 1957) and ‘psychomotor retardation’ (Deniker, 1960) antipsychotics produced based on detailed observations of how they affected people.

Understanding the effects of antipsychotics in this way is important because it explains why taking them can be so unpleasant for users, and makes sense of data suggesting that taking antipsychotics over the long-term can incur neurotoxicity as manifested in tardive dyskinesia and brain volume reduction (Moncrieff & Leo, 2010), and impair social functioning (Wunderink, Nieboer, Wiersma, Sytema, & Nienhuis, 2013). Therefore, although we concur that antipsychotics can be useful treatments for acute psychosis, it is essential to ensure that they are not over-used, and that the balance of benefits and harms has been carefully and thoroughly researched in all situations, but especially in relation to long-term use.

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