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Reducing long-term antipsychotic use: a therapeutic dead end?

Murray and colleagues' confident advice[1] to psychiatrists, encouraging them to leave fewer patients with schizophrenia on long-term medication, is based on one of several possible interpretations of a selected literature, and little clinical evidence. We consider that at times Murray and colleagues misrepresented the literature in their descriptions of what some papers report; sometimes these descriptions are misleading (e.g. their references to Mace *et al* (2015), Vita *et al* (2015) and Boonstra *et al* (2011)) or incorrect (Saha *et al* (2007)). If the evidence so strongly supports the authors' recommendations, why have they relied so heavily on single case reports and personal communications, and on qualifying words such as 'doubts', 'possibilities', 'suggest', 'appear', 'raise the possibilities', 'several Japanese groups have suggested'? Why have they given prominence to a study (Harrow *et al* (2014)) that they admit has a 'major confounder', and another (Wunderink *et al* (2013)) that they describe as 'a study less open to bias', which others consider grossly flawed (reviewed by Catts & O'Toole[2])? And why do they consistently refer to use of low or no doses, without ever describing the conditions that discriminate these indications?

Murray and colleagues assert that continuous antipsychotic medication loses its effectiveness over time, but do not present any clinical evidence for this, and that this putative treatment resistance is due to antipsychotic-induced dopamine receptor supersensitivity that has been found in animal studies. Indeed, the authors rely heavily on animal studies generally to make their case for a range of issues, without highlighting the fact that the relevant animal studies were all carried out on healthy animals. The authors seem overly confident that the results of these animal studies can be applied directly to the clinical situation, although no psychiatrist uses antipsychotic medication in healthy humans. The authors fail to see the complete disconnect between healthy animal research and clinical research on patients with schizophrenia. It seems to us that the reliance on animal studies by Murray and colleagues has resulted in their treatment recommendations being almost the opposite of others based on clinical literature.[2]

We suggest that Murray and colleagues are proposing a therapeutic dead end. With current practice, most patients stop their medication anyway (mainly owing to non-adherence to oral medication) – 60% of patients with first-episode psychosis do so within 60 days of hospital discharge:[3] so how will taking more patients off their antipsychotic medication improve the current overall recovery rates in schizophrenia of 13.5%,[4] and the death rates that all agree are unacceptably high? Murray and colleagues' answer is more psychosocial intervention, but they present no evidence for the effectiveness of such intervention in unmedicated patients. The clinical evidence for antipsychotic medication reducing the mortality rate at all stages of the illness is of high quality and very consistent (summarised by Tiihonen[5]); the simple truth is that taking more patients off maintenance medication will result in more patients dying unnecessarily – the ultimate therapeutic dead end.

Declaration of interest

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1 Murray RM, Quattrone D, Natesan S, van Os J, Nordentoft M, Howes O, et al. Should psychiatrists be more cautious about the long-term prophylactic use of antipsychotics? *Br J Psychiatry* 2016; **209**: 361–5.

2 Catts SV, O'Toole BI. The treatment of schizophrenia: can we raise the standard of care? *Aust NZ J Psychiatry* 2016; **50**: 1128–38.

3 Tiihonen J, Haukka J, Taylor M, Haddad PM, Patel MX, Korhonen P. A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia. *Am J Psychiatry* 2011; **168**: 603–9.

4 Jaaskelainen E, Juola P, Hirvonen N, McGrath JJ, Saha S, Isohanni M, et al. A systematic review and meta-analysis of recovery in schizophrenia. *Schizophr Bull* 2013; **39**: 1296–306.

5 Tiihonen J. Editorial: real-world effectiveness of antipsychotics. *Acta Psychiatr Scand* 2016; **134**: 371–3.

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Bipolar affective disorder and childhood adversity: possible genetic links?

Palmier-Claus *et al*[1] appear to conclude from their meta-analysis that childhood adversity is clearly, and independently, linked to developing bipolar disorder as an adult.

Surely, however, adults with bipolar disorder are hugely more likely than healthy population controls to have had parents (and other relatives) who themselves suffered from affective disorders, given the genetic heritability of these illnesses. It is surely accepted that affective disorders in parents have a negative effect on the well-being of children, and the adversity experienced by children may (at least in part) be mediated by affective disorders in their parents.

To ignore the possible effect of experiencing adverse events in childhood precisely because there was a greater likelihood of affective disorder among these children's parents seems to me to be a glaring omission in this paper.

1 Palmier-Claus JE, Berry K, Bucci S, Mansell W, Varese F. Relationship between childhood adversity and bipolar affective disorder: systematic review and meta-analysis. *Br J Psychiatry* 2016; **209**: 454–9.

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