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Letter to the editor

To the editor

Abi-Dhargham et al. (Eur. Psychiatry 20 (2005) 15) comprehensively review the contribution of brain imaging to understanding the mechanism of second generation antipsychotic drugs. The review touches on our findings showing that all the second generation drugs we studied with 123I epidepride single photon emission tomography (SPET) preferentially block D2/D3 dopamine receptors in the temporal cortex, vs. striatum (Pilowsky et al., 1997; Bigliani et al., 2000; [5]; [2]). They go on to state these findings must be viewed 'with caution' since the 'simple ratio method' was used to determine specific D2/D3 binding in striatum and temporal cortex. It is important to correct factual errors that by unchallenged repetition in respected journals, gain credibility. We addressed the issue of inaccuracies associated with the ratio method by simulation and experiment 2003 [3], and showed that though the ratio method could underestimate striatal D2/D3 receptor occupancy, it was accurate in the temporal cortex for the timescale of an epidepride SPET experiment. The short timescale of 11C FLB 457 PET experiments conversely could lead to an underestimation of temporal cortical D2/D3 receptor occupancy in this area, and a mistaken acceptance that there is no difference in striatal vs. limbic cortical occupancy by second generation antipsychotic drugs, especially when two different PET ligands are used to estimate occupancy in each area. PET studies addressing this issue use a long-lived isotope (18F or Br76), and label D2/D3 receptors in striatal and extra-striatal regions at the same time in the same experiment [4,7]. These studies report similar results to our own. We also used reference tissue modelling and 123I epidepride SPET to show the chemically distinct atypical antipsychotic drugs amisulpride and risperidone preferentially block D2/D3 receptors in limbic cortical, over striatal regions [1,2]. Furthermore, within the striatum, D2/D3 receptor occupancy by risperidone and amisulpride was higher in the head of caudate (limbic cortical associative inputs) than putamen (mainly motor connections) [6]. It is worth noting that these findings are dose-dependent for drugs with relatively high affinity for the D2 receptor, so that 'limbic selectivity' disappears at higher plasma levels, and all PET and SPET D2/D3 occupancy studies should be viewed with this in mind.

Notes added in proof.

References

[1] Bressan RA, Erlandsson K, Jones HM, Mulligan RS, Ell PJ, Pilowsky LS. Optimizing limbic selective D2/D3 receptor occupancy by risperidone: a [123I]-epidepride SPET study. J Clin Psychopharmacol 2003;23(1):5–14.
[2] Bressan RA, Erlandsson K, Jones HM, Mulligan R, Flanagan RJ, Ell PJ, et al. Is regionally selective D2/D3 dopamine occupancy sufficient for atypical antipsychotic effect? An in vivo quantitative [123I]epidepride SPET study of amisulpride-treated patients. Am J Psychiatry 2003;160(8):1413–20.
[3] Erlandsson K, Bressan RA, Mulligan RS, Ell PJ, Cunningham VJ, Pilowsky LS. Analysis of D2 dopamine receptor occupancy with quantitative SPET using the high-affinity ligand [123I]epidepride: resolving conflicting findings. Neuroimage 2003;19(3):1205–14.
[4] Grunder G, Landvogt C, Vernaleken I, Buchholz G, Ondracek J, Siessmeier T, et al. The striatal and extrastriatal D2/D3 receptor-binding profile of clozapine in patients with schizophrenia. Neuropsychopharmacol 2005;30 epub ahead of print.
[5] Stephenson CM, Bigliani V, Jones HM, Mulligan RS, Acton PD, Visvikis D, et al. Striatal and extra-striatal D(2)/D(3) dopamine receptor occupancy by quetiapine in vivo. [(123)I]-epidepride single photon emission tomography (SPET) study. Br J Psychiatry 2000;177:408–15.
[6] Stone JM, Bressan RA, Erlandsson K, Ell PJ, Pilowsky LS. Non-uniform blockade of intrastriatal D(2)/D(3) receptors by risperidone and amisulpride. Psychopharmacology (Berl) 2005;180:664–9.
[7] Xiberas X, Martinot JL, Mallet L, Artiges E, Loc'H C, Maziere B, Paillere-Martinot ML. Extrastriatal and striatal D(2) dopamine receptor blockade with haloperidol or new antipsychotic drugs in patients with schizophrenia. Br J Psychiatry 2001;179:503–8.

Lyn S. Pilowsky*
KCL Institute of Psychiatry,
UCL Department of Psychological Medicine,
Honorary Professor Institute of Nuclear Medicine, Box 54,
De'Crespigny Park, London SE5 8AF, UK
E-mail address: l.pilowsky@iop.kcl.ac.uk (L.S. Pilowsky).

James M. Stone
Department of Psychological Medicine,
KCL Institute of Psychiatry, Box 54,
De'Crespigny Park, London SE5 8AF, UK
E-mail address: j.stone@iop.kcl.ac.uk (J.M. Stone).

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*Corresponding author.

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