Neuropsychopharmacology (2006) 31, 244–245

www.neuropsychopharmacology.org

Reply to Doraiswamy

Reply: Atypical Antipsychotics and Pituitary Size

Carmine M Pariante*[,1] and Paola Dazzan[1]

[1]*King's College London, Division of Psychological Medicine, Institute of Psychiatry, London, UK*

Neuropsychopharmacology (2006) **31,** 244–245. doi:10.1038/sj.npp.1300904

Sir

We are delighted that Dr Doraiswamy, while commending our study on pituitary volume in first-episode psychosis (Pariante *et al*, 2005), has provided stimulating comments and queries regarding antipsychotic-induced hyperprolactinemia. In order to address some of Dr Doraiswamy's concerns, we have further examined the sample described in the paper. Moreover, we have reviewed all our studies on pituitary volume in psychosis in the light of his comments (Garner *et al*, 2005; Pariante *et al*, 2004; Pariante *et al*, 2005).

Dr Doraiswamy is concerned that we may have underestimated the effects of past use of typical antipsychotics on pituitary volume in the patients defined as 'drug-free' (ie, drug-free for at least 3 weeks) or 'on atypicals' (ie, on atypicals for the last 2 weeks). Theoretically, it is possible that the pituitary volume of patients who had taken typicals prior to their current treatment would not decrease in the 2–3 weeks they had been drug-free or on atypicals. However, it is important to highlight that most of the subjects in the 'drug-free' group (12 out of 18, 67%) were antipsychotic-naïve, and the others had previously received a typical for a very short period of time (two for 2–3 days, and one for 20 days). Similarly, most subjects in the 'atypicals' group had received only one or two doses of a typical in the past (20 out of 26, 77%), and other five subjects had received a typical in the past for 1 or 2 weeks only. Indeed, we believe that the most striking evidence in support to the hypothesis that the enlargement of the pituitary in the 'drug-free' and 'atypicals' subjects is due to activation of ACTH-producing cells by the stress response (rather than to antipsychotic-induced stimulation of prolactin) is that a similar enlargement is present in the 12 antipsychotic-naïve subjects (Pariante *et al*, 2005). Moreover, a similar enlargement of the pituitary gland is also present in antipsychotic-naïve prodromal subjects from the PACE Clinic in Melbourne, before they develop psychosis (Garner *et al*, 2005).

Of course, Dr Doraiswamy is correct in saying that our study could not detect potential differences between different atypicals in their effects on pituitary volume, because most of the subjects on atypicals were receiving olanzapine (Pariante *et al*, 2005). Indeed, it is possible that risperidone and amisulpride have an effect on pituitary volume that is similar to that of typicals. Although we do not have enough subjects for such a comparison in this study, it is interesting to note that our previous study in an Australian sample of patients with first-episode psychosis (where the pituitary volume was also enlarged) found no difference in pituitary volume between subjects on typicals and subjects on atypicals who were mostly receiving risperidone (Pariante *et al*, 2004).

Following Dr Doraiswamy's suggestion, we have further examined the interaction between gender and antipsychotic treatments in the regulation of pituitary volume. Pituitary volume is generally larger in females than males, and this gender effect is present in both patients and controls (Pariante *et al*, 2005). However, we have now found in this sample that subjects on atypical do not present this gender difference (unpublished data). While the small numbers of subjects prevents any speculation on this finding, it is interesting to note that we have previously reported a lack of gender difference in pituitary volume in patients with established psychosis, half of whom were on clozapine (Pariante *et al*, 2004). Therefore, it is possible that typical and atypical have different effects on pituitary volume that go beyond prolactin secretion and may involve other hormones that regulate the stress, sexual and metabolic function. Indeed, a separate study on the present sample has demonstrated that typical and atypical antipsychotics have different structural effects on a variety of brain regions (Dazzan *et al*, 2005). In the future, we will also be able to comment on the genetic regulation of pituitary volume, thanks to studies that are currently ongoing in our Institute.

*Correspondence: Dr CM Pariante, King's College London, Section of Clinical Neuropharmacology, PO51, Institute of Psychiatry, 1 Windsor Walk Denmark Hill, London SE58AF, UK, Tel: +44 20 7848 0807, Fax: +44 20 7848 0051. E-mail: c.pariante@iop.kcl.ac.uk
Received 12 August 2005; accepted 17 August 2005
Online publication: 19 August 2005 at http://www.acnp.org/citations/Npp081905050498/default.pdf

Finally, with the emerging evidence linking psychosis and antipsychotics with metabolic abnormalities, we endorse Dr Doraiswamy's view that more work into the long-term pathological consequences of hyperprolactinemia is urgently needed.

REFERENCES

Dazzan P, Morgan KD, Orr KG, Hutchinson G, Chitnis X, Suckling J *et al* (2005). Different effects of typical and atypical antipsychotics on grey matter in first episode psychosis: the ÆSOP study. *Neuropsychopharmacology* **30**: 765–774.

Garner B, Pariante CM, Wood SJ, Velakoulis D, Phillips L, Soulsby B *et al* (2005). Pituitary volume predicts future transition to psychosis in individuals at ultra-high risk of developing psychosis. *Biol Psychiatry* **58**: 417–423.

Pariante CM, Vassilopoulou K, Velakoulis D, Phillips L, Soulsby B, Wood SJ *et al* (2004). Pituitary volume in psychosis. *Br J Psychiatry* **185**: 5–10.

Pariante CM, Dazzan P, Danese A, Morgan KD, Brudaglio F, Morgan C *et al* (2005). Increased pituitary volume in antipsychotic-free and antipsychotic-treated patients of the AEsop First-Onset Psychosis Study. *Neuropsychopharmacology*, June 1 [Epub ahead of print].