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Letter to the Editor

Increased Pituitary Volume in …Psychosis Study

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Sir

I commend Pariante *et al* (2005) on their MRI study of pituitary volume in psychosis. Their finding that pituitary volume is increased in depression is consistent with prior studies from Duke more than a decade ago (Krishnan *et al*, 1991). The finding that typical antipsychotics increase pituitary size due to stimulation of lactotroph proliferation is quite important since prior case reports as far back as 20 years ago have studied antipsychotic links to pituitary microadenomas (Asplund *et al*, 1982).

However, readers should be aware that the Pariante *et al* study may have inadvertently underestimated the pituitary effects of some atypical antipsychotics for several reasons. First, a third of their 'untreated' patients had previously received antipsychotics although they were free of antipsychotics for atleast 3 weeks. While a 3-week washout may be sufficient to lower prolactin levels, it is not known if a 3-week washout is sufficient to reverse pituitary gland enlargement or possible microadenomas. Microadenomas smaller than 5 mm may not be detected by MRI, especially if gadolinium contrast was not done. In mice, promotion of pituitary cell proliferation with antipsychotics is a chronic effect seen over 18–24 months (Studies described in package inserts of antipsychotic drugs, www.risperdal.com; www.sanofi-synthelabo.com.au/pdf/Solian%20Pl.doc; accessed August 2005) and some human microadenomas only reverse after months of treatment with dopamine agonists. Second, the study pooled all atypical agents although data suggests that some atypicals (eg risperidone, amisulpride) may be more potent than others at stimulating prolactin from the pituitary (Haddad and Wieck, 2004). Nearly 75% (19 of 26) of their atypical subjects were on olanzapine and hence it is not clear if their finding can be generalized to all atypical antipsychotics. Further, since only a 2-week exposure was required to meet criteria for 'atypical treatment', this may have resulted in underestimating chronic effects of pituitary stimulation. Lastly, there are likely gender and genotype related differences in antipsychotic effects on the pituitary lactotrophs (Haddad and Wieck, 2004; Young *et al*, 2004), which were not fully explored in this study.

Given the logistics and expenses of conducting an MRI study in psychotic subjects, the issues raised by me are not meant to dimish the value of this pioneering study but to stimulate further debate. Given that dopamine antagonism stimulates lactotroph proliferation, it is likely that any potent dopamine antagonist will affect pituitary size more so than a less potent antagonist. Prospective direct comparison studies of atypical antipsychotcs looking at the long-term consequences of hyperprolactinemia would be insightful.

DISCLOSURE

I have received research grants and honoraria (consulting, speaking) from several pharmaceutical companies including the manufacturers of the products discussed in this letter. I do not own stock in any of these companies.

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