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Letter to the Editor

Plasma Leptin and Antipsychotic-Induced Body Weight Gain

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Sir

We read with interest the paper by Dr Haupt and co-workers (which appeared in a recent issue of the journal, 2005) concerning the putative role of leptin in the antipsychotic-induced body weight (BW) gain. Those authors performed a cross-sectional study measuring plasma leptin concentrations in schizophrenic patients treated with olanzapine, risperidone, or typical antipsychotics as compared to drug-free healthy controls. Since adiposity-related elevations in circulating leptin concentrations were similar in antipsychotic-treated patients and drug-free healthy controls, the authors concluded that antipsychotics-induced BW gain is not associated with defects in leptin secretion, clearance, or signaling. However, as Dr Haupt and co-workers pointed out in the discussion, their study '*did not collect prospective serial measurements of changes in plasma leptin during the initial phase of antipsychotics treatment, limiting the ability to rule out changes in leptin signaling that might occur early in the process of weight change*'.

Actually, 3 years ago, we performed exactly such a kind of prospective study (Monteleone *et al*, 2002) and provided the evidence that in patients with schizophrenia, after 2 weeks of clozapine administration, plasma leptin levels increased much more than the amount of weight gained by patients and this increase negatively correlated with the patients' percent increases of BW after 6 and 8 months of treatment. We hypothesized that, in the first phase of clozapine treatment, the marked rise in circulating leptin independently of total BW changes could theoretically signal to the brain the immediate need for appetite suppression and/or increase in the energy expenditure to counteract the incoming disturbance of the metabolic state induced by clozapine. This acute signaling function of leptin likely has long-term effects, since the higher the increase in the fat hormone plasma levels after 2 weeks of treatment, the lower the weight increase gained by clozapine-treated patients after 6 and 8 months of treatment.

Therefore, taking into account our results and those of Haupt *et al*, it seems that in patients experiencing antipsychotic-induced BW gain not only there is no impairment of leptin physiology, but circulating leptin changes in the first phase of treatment are likely to have even a protective role against long-term induced BW gain.

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There is no conflict of interest with this letter.

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