Neuropsychopharmacology (2006) 31, 2328

www.neuropsychopharmacology.org

Reply to Elman *et al*

Is There Such Thing as a Schizophrenic Stomach?

Igor Elman*[,1], David Borsook[2] and Scott E Lukas[1]

[1]*Department of Psychiatry, Behavioral Psychopharmacology Research Lab., McLean Hospital, Harvard Medical School, Belmont, MA, USA;* [2]*PAIN Group, McLean Hospital and Harvard Medical School, Belmont, MA, USA*

Neuropsychopharmacology (2006) **31**, 2328. doi:10.1038/sj.npp.1301141

Sir

We appreciate Drs Treuer and Karagianis interest in our work and their underscoring yet again the apparent complexity and multidisciplinary nature of the weight gain problems in patients with schizophrenia. The assertion that these problems may arise due to increases in ghrelin secretion from the stomach produced by the second-generation antipsychotic agents (SGAs) is however undermined by the following considerations: (a) preponderance of the studies reporting no or inverse relationship between plasma ghrelin levels and SGAs-induced weight gain (Togo *et al*, 2004; Palik *et al*, 2005; Theisen *et al*, 2005; Sporn *et al*, 2005; Hosojima *et al*, 2006); (b) the lack of reported evidence on ghrelin alterations in drug-free patients who are also prone for glucoregulatory abnormalities and for obesity; and (c) undetermined (primary *vs* secondary) mechanisms of the SGAs ghrelin effects. We have discussed the inconclusive ghrelin findings in the text (page 15) and in the tabulated format (Elman *et al*, 2006).

Nonetheless the letter by Drs Treuer and Karagianis raises an important question concerning reciprocity between central nervous system and gastrointestinal (GI) pathologies, the entity addressed by the discipline of neurogastroenterology. Indeed, embryonically, the central and the enteric nervous systems are derived from the same neural crest tissue and are subsequently linked via the vagus nerve. Furthermore, the GI tract is abundant with the same hormones and neurotransmitters that are mediating reward and homeostatic processes in the brain; to name a few, cholecystokinin, insulin, opiates, gamma-aminobutyric acid, dopamine, serotonin, glutamate, and norepinephrine. The GI concentrations of these chemicals are comparable to or are even exceed those in the brain (Gershon, 1998). Hence, it is in the realm of possible that the same prenatal lesion driving the development of schizophrenia neuropathology (Weinberger, 1987) may also result in corresponding alterations of the GI system, including impaired regulatory mechanisms of ghrelin secretion. Such a concept could gain indirect support from high prevalence of celiac disease in schizophrenic patients and their first-degree relatives (Eaton *et al*, 2004, 2006). In more general terms, the dynamic view of the brain–periphery interactions, rather than an either/or approach to the ailments afflicting both domains may provide heuristic value to clinical neuroscience and bring us closer to solving the mind–body mystery.

In sum, although available clinical evidence renders elevated ghrelin an unlikely cause of weight gain during SGAs therapy, further research in this area is warranted.

*Correspondence: Dr I Elman, Department of Psychiatry, Behavioral Psychopharmacology Research Lab., McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, USA, Tel: +1 617 8553692, Fax: +1 617 855 3711, E-mail: ielman@partners.org
Received 19 May 2006; accepted 25 May 2006
Online publication: 31 May 2006 at http://www.acnp.org/citations/Npp053106060331/default.pdf

REFERENCES

Eaton W, Mortensen PB, Agerbo E, Byrne M, Mors O, Ewald H (2004). Coeliac disease and schizophrenia: population based case control study with linkage of Danish national registers. *BMJ* **328**: 438–439.

Eaton WW, Byrne M, Ewald H, Mors O, Chen CY, Agerbo E (2006). Association of schizophrenia and autoimmune diseases: linkage of Danish national registers. *Am J Psychiat* **163**: 521–528.

Elman I, Borsook D, Lukas SE (2006). Food intake and reward mechanisms in patients with schizophrenia: implications for metabolic disturbances and treatment with second-generation antipsychotic agents. *Neuropsychopharmacology* (in press).

Gershon M (1998). *The Second Brain*. HarperCollins: New York, NY.

Hosojima H, Togo T, Odawara T, Hasegawa K, Miura S, Kato Y *et al* (2006). Early effects of olanzapine on serum levels of ghrelin, adiponectin and leptin in patients with schizophrenia. *J Psychopharmacol* **20**: 75–79.

Palik E, Birkas KD, Faludi G, Karadi I, Cseh K (2005). Correlation of serum ghrelin levels with body mass index and carbohydrate metabolism in patients treated with atypical antipsychotics. *Diabetes Res Clin Pract* **68**: S60–S64.

Sporn AL, Bobb AJ, Gogtay N, Stevens H, Greenstein DK, Clasen LS *et al* (2005). Hormonal correlates of clozapine-induced weight gain in psychotic children: an exploratory study. *J Am Acad Child Adolesc Psychiat* **44**: 925–933.

Theisen FM, Gebhardt S, Bromel T, Otto B, Heldwein W, Heinzel-Gutenbrunner M *et al* (2005). A prospective study of serum ghrelin levels in patients treated with clozapine. *J Neural Transm* **112**: 1411–1416.

Togo T, Hasegawa K, Miura S, Hosojima H, Kojima K, Shoji M *et al* (2004). Serum ghrelin concentrations in patients receiving olanzapine or risperidone. *Psychopharmacology (Berlin)* **172**: 230–232.

Weinberger DR (1987). Implications of normal brain development for the pathogenesis of schizophrenia. *Arch Gen Psychiat* **44**: 660–669.