Author’s response to reviews

Title: Tyrosine hydroxylase activity in the endocrine pancreas: changes induced by short-term dietary manipulation

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La Plata, December 27, 2002.

Clare Collett, PhD
Assistant Editor
BMC Journals

Dear Mrs. Collett:

We have carefully read the comments of the two reviewers. Accordingly, we have introduced changes in the manuscript and have the following comments:

Reviewer Dr Sue Chan
Advice on publication: Opposed to her opinion, we believe that our study merits publication because:

a) It demonstrates for the first time the measurable presence of TH activity in islets and its modulation by dietary manipulation, b) It provides evidence of its origin in islet tissue and of a possible feedback mechanism for the control of TH activity, and c) The coincidence of increased TH activity with decreased release of insulin in response to glucose in vivo and in vitro.

1. We included duration of the experiment in Material and methods: page 4, line 8.
2. It has been reported that a sucrose-rich diet increases the sympathetic activity and NE turnover in pancreatic and other tissues [Young JB et al, Am J Physiol 1979, 236: E524-E533] in man and rats [Landsberg L et al, Metabolism 1980, 29: (Suppl 1):1128-1137]. This diet has been used as a tool to assess whether changes in CAs metabolism affects a given function, in our case insulin secretion. Physiological significance can be drawn from the analysis of the data obtained. In our case, we included the issue in the Discussion and Conclusions.
3. The caloric content of the diets was included: page 6, lines 18 to 19.
4. Although significantly higher than in control rats, blood glucose levels in CHD-fed animals were within the normal range, thus, there is no experimental evidence to ascribe our results to glucose desensitization, glucose toxicity or B-cell exhaustion.
5. We have previously reported the effect of a specific TH inhibitor upon in vitro insulin secretion. Therefore, even when we could perform the experiment suggested by the reviewer, we believe that it would not add critical support to the current results.
On the other hand, our group has also reported CAs effect upon basal insulin secretion (Horm Metab Res 2: 317-322, 1970).
Regarding the relationship between increased TH activity and decreased release of insulin in response to glucose, we considered TH activity as an indicator of CAs biosynthesis.
6. The effect of a long period of low protein intake upon insulin secretion (Acta Physiol Latinoam 20: 50-57, 1970) is known. But we believe that its discussion, further than its mentioning as a possibility
to affect insulin secretion in our model, is beyond the scope of the study.

Reviewer Prof. Peter Thams
1. We agree on the importance of this study. But we are unable at the moment to measure TH activity and CAs content; thus, we cannot perform the requested experiment.
2. Insulin content in islets was included (Figure 2, inset, page 5, lines 3 to 6 and page 7, lines 8 to 10) Accordingly, the decreased release of insulin by islets from CHD-fed rats cannot be ascribed to insulin content, since their values were higher than those found in control animals (page 8, lines 10 to 13).
3. Islet CAs content has been included (page 6, lines 4 to 10 and page 7, line 3 and 4). The effect of adrenergic antagonists has been also discussed (page 3, lines 14 to 16).
4. The abstract in Diabetologia is quoted (reference 24).

We hope that the changes introduced and the comments included in this letter can overcome the reviewers requests, making the manuscript acceptable for publication.

Looking forward to your news, we remain,

Yours,

Dr. JJ Gagliardino