Reviewer's report

Title: Xylazine-induced Reduction of Tissue Sensitivity to Insulin Leads to Acute Hyperglycemia in Diabetic and Non-diabetic Monkeys

Version: 2 Date: 24 September 2013

Reviewer: Shiro Kurusu

Reviewer's report:

Reviewer’s response: I still have some doubts about the first major issue. The authors’ conclusion that the primary cause is the reduced sensitivity to insulin is supported only by the last result. Neither the first nor the second result supports their claim, because it could be explained that xylazine may increase blood glucose through up-regulation of glucose-increasing hormone(s) which the authors could not find here. Compared to blood glucose data, those of insulin and other hormones seem very variable and thus may have produced the authors’ conclusion of no significant changes in these glucose regulators.

As was described, increase in blood glucose induced by this anesthetic had previously been in several animal species. This work only confirmed the phenomenon in non-human primate with additional suggestion that the cause is possibly the reduced sensitivity to insulin. I meant insulin by “the hormone” and still strongly believe that another data of some change(s) in insulin signaling pathways should increase the value of this paper. This issue is never out of the concern of general readers. I do not support the idea “one paper, one (or two) novel finding”.

The reviewer accepts other revisions and claims.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.