



SDI FINAL EVALUATION FORM 1.1

PART 1:

Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	MS: 2012 IJBcRR 2833
Title of the Manuscript:	Hormonal Sensitivity of Adenylyl Cyclase in the Myocardium, Brain and Testes of 18-month-old Non-Diabetic and Diabetic Rats

PART 2:

FINAL EVALUATOR’S comments on revised paper (if any)	Authors’ response to final evaluator’s comments
- There would seem to be a not close relation between the tissues observed in the present study. The authors have yet to explain the reasons clearly that why were the tissues chosen as of this study. - It is well known that the main complications of the disease include cardiovascular and cerebrovascular disease, neuropathy, retinopathy, and nephropathy, etc. Heart disease and stroke are the leading causes of death in these patients. As so far, the male infertility problem the authors mentioned is not one of the main complications. - The review (reference 22) cited by the authors is not concerning impact of diabetes on the male infertility. - The data of alterations of cardiac function and the fertility with age also should be presented, so as to obtain further direct evidence, authors could confirm relation between the hormone-sensitive AC system and cardiac and genital dysfunction in the animals.	1. The choice of the tissues observed in the study was determined by the following reasons: (i) The impairment in functioning of the diabetic brain is one of the key causes of dysfunctions in the peripheral systems, including the cardiovascular and the reproductive systems; (ii) The attenuation of functional activity of HHG axis in diabetes, metabolic syndrome and aging induces cardiovascular diseases, while the abnormalities of the cardiovascular system and the peripheral circulation can cause the impairment of reproductive functions (Moyad MA. Heart health = urologic health and heart unhealthy = urologic unhealthy: rapid review of lifestyle changes and dietary supplements. Urol Clin North Am. 2011 Aug;38(3):359-67; Abadilla KA, Dobs AS Topical testosterone supplementation for the treatment of male hypogonadism. Drugs. 2012 Aug 20;72(12):1591-603; and other works). Thus, the selected tissues are functionally linked. (iii) The cardiovascular and reproductive diseases are one of the most frequent complications of T2DM, and the study of possible molecular mechanisms of their development is one of the efficient ways to treat these complications. (iv) The adenylyl cyclase signaling system in the brain, myocardium and testes of experimental animals and human with long-term type 2 diabetes was not studied before our work. In the case of other diabetic models and in control animals we well-studied AC system in these tissues. We changed two sentences in the last paragraph of Introduction section: The text “Clinical studies show that diabetic cardiomyopathy is a leading cause of death of diabetic patients, and also demonstrate the relationship between male infertility and T2DM-induced hypogonadotrophic hypogonadism and spermatogenic failure [22,26,27]” was replaced by “Clinical studies show that diabetic cardiomyopathy is a leading cause of death of diabetic patients [26,27]. The close link between male infertility and T2DM-induced hypogonadotrophic hypogonadism and spermatogenic failure was also found [22,28,29]”. 2. According to the second comment, we changed the first phrase in the Introduction. The text “The type 2 diabetes mellitus (T2DM) leads to severe complications in the nervous, cardiovascular and reproductive systems, which is a result of the impairment of lipid and carbohydrate metabolism, endothelial dysfunction, as well as the alterations in the hormonal signaling systems of the brain and peripheral tissues” was replaced by the text “The type 2 diabetes mellitus (T2DM) leads to severe complications that include cardiovascular dysfunctions, neurodegenerative diseases, nephropathy, retinopathy, and neuropathy. The dysfunctions in the male reproductive system are also common in T2DM and cause male infertility and psychological and psychosocial problems. These complications are the result of the impairment of lipid and carbohydrate metabolism, endothelial dysfunction, as well as the alterations in the hormonal signaling systems of the brain and peripheral tissues”. 3. We replaced the review of Mah PM and Wittert GA (Reference 22), which includes the analysis of male infertility in obesity, metabolic syndrome and type 2 diabetes, to more appropriate articles devoted to the impairment of reproductive functions and spermatogenesis in type 2 diabetes mellitus (Ref 22: La Vignera S, Condorelli R, Vicari E, D'Agata R, Calogero AE. Diabetes mellitus and sperm parameters. 2012;33:145-53. doi: 10.2164/jandrol.111.013193; Ref 28: Mallidis C, Agbaje I, McClure N, Kliesch S.The influence of diabetes

	mellitus on male reproductive function: a poorly investigated aspect of male infertility. Urologe A. 2011;50:33-7. doi: 10.1007/s00120-010-2440-3; Ref 29: Isidro ML. Sexual dysfunction in men with type 2 diabetes. Postgrad Med J. 2012 Mar;88(1037):152-9. doi: 10.1136/postgradmedj-2011-130069). 4. We are grateful for the valuable proposals for the physiological aspects of the study of the cardiovascular and reproductive systems in experimental T2DM and aging. In the future, we plan to study the alterations of physiological functions of the reproductive and the cardiovascular systems in aging rats with neonatal diabetes, and compare the dynamics and severity of these alterations with the biochemical data on the adenylyl cyclase system obtained in this study. However, both ideologically and methodologically, it is a different (physiological) study.
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