

Article information: <http://dx.doi.org/10.21037/atm-19-4534>

Comment: How were the two groups of SD rats divided? Were the two groups divided before or after the injection of STZ? What treatment did the control group receive?

Response: We are sorry that the groups were not explained clearly in paper. So, we make some corrections in the description of grouping in revised paper. Please see **Page 2, line27 and Page 5, line257-261**. Firstly, we divided them into diabetic group (n=18) and control group (n=6) before the injection of STZ. Then, the diabetic group were divided into subgroups of diabetic nerve compression 2 weeks (DNC2W, n=6), 4 weeks (DNC4W, n=6), and 8 weeks (DNC8W, n=6) according to the time of nerve compression. Considering our purpose is to investigate the evaluation of diabetic nerve compression before treatment, we did not give any treatments to the control group. But your valuable comment gives us the precious enlightenment to investigate the value of elastography in follow-up after treatment of diabetic nerve compression in our further research.

Comment: In the paper, the left hind limb of rats was exposed and damaged. Why did the experiment not involve both hind limbs? When the left hind limb was damaged, the right hind limb was vicarious function.

Response: We appreciated your comments about the right sciatic nerve in diabetic rats. We have evaluated the right sciatic nerve by SWE (**Please see Page5, line260-261**), and added the graph and data in paper, **please see Figure 1(D-F) and table 1 (DM2W, 4W and 8W)**. And the text description of the results were added at **Page9, line465-467**. We want to explain about the supplementary data and would like to ask for your precious suggestions. Vicarious function occurs mostly in tissues with strong regeneration ability. Nerve regeneration ability is so weak that the emerge of vicarious function on nerve may be need a very long time. Eight weeks might be a relatively short time. Also, there was rarely reported that the contralateral nerve vicarious function after diabetic nerve compression 8 weeks in literatures. And there is no differences were found by SWE in right sciatic nerve in diabetic rats at different times in our paper. Moreover, the diabetic neuropathy is a polyneuropathy. Bilateral sciatic nerves can be reflected by diabetic

mellitus. Although the damage could accelerate the process of diabetic neuropathy at left sciatic nerve, the right nerve also under a risk of diabetic neuropathy. So, we consider the right sciatic nerve in under the condition of DM over the vicarious function.

Comment: Figures 1-3 are not clear enough. Please provide clearer figures.

Response: New clearer figures have been uploaded. Hope them can present better and meet the requirement. If there are still shortcomings, we are willing to make further modifications.

Comment: Please provide the graph of the sciatic nerve of the rats at 2 weeks, 4 weeks, and 8 weeks. Also, what was the blood glucose concentration of the rats at 2 weeks, 4 weeks, and 8 weeks?

Response: We added the the graph of the sciatic nerve of the normal and diabetic rats at 2 weeks, 4 weeks, and 8 weeks in revised paper, please see **Figure 1 (A-F)**. Also, the blood glucose concentration of the rats at 2 weeks, 4 weeks, and 8 weeks are added. Please see **Page9, line469-471**.

Comment: Why were the myelinated fibers not identified using immunohistochemistry?

Response: We did the quantitative analysis of myelinated fibers. The myelin sheath can be dyed specifically by methods of OsO₄ staining and toluidine blue staining. Moreover, these two methods have been accepted as conventional quantitative methods in academic research. Immunohistochemistry as a semi-quantitative method for proteins can quantify the myelinated fiber, and S100 is one of the most commonly test index. Then according to some literatures, we found that the immunohistochemistry was more used in research of follow-up after treatment of diabetic neuropathy in recent years. The treatment of diabetic neuropathy remains a challenge, so we consider that the test of protein level may be more meaningful in research of diabetic neuropathy after treatment. Meanwhile, the more complex operating procedures and the higher cost make it difficult to our team. After comprehensive consideration, we think the degree of nerve lesion would be well reflected by method of quantitative morphometry on histological level, as to verify the value of elastography. We appreciate your comment on our study in terms of immunohistochemistry. Neuroscience is a complex subject, more in-depth research needs

to continue in future, we are willing to consider adding immunohistochemistry in future study, especially in research of treatments for diabetic neuropathy.

Comment: Figure 1 is missing statistics. Please include these.

Response: We are sorry for our negligence of missing statistics in Figure 1. We have added the missing statistics in new **Table 1**. Please see **Table 1**.

Comment: Why were myelinated fibers tested? The relevant content about myelinated fibers is missing from the title and conclusions in the paper.

Response: It is well established that diabetic neuropathy is characterized by both myelinated and unmyelinated nerve fiber degeneration and regeneration, and mainly involved myelinated fibers. [*Bibliography: Brussee V, Guo G, Dong Y, et al. (2008) Distal degenerative sensory neuropathy in a long-term type 2 diabetes rat model. Diabetes 57(6):1664–1673*]. One of the remarkable features on diabetic neuropathy is the decline of the density of myelinated fibers, and it relates best to peripheral nerve electrophysiology, but unmyelinated fibre has a poor relationship to peripheral nerve electrophysiology of unmyelinated nerve fibers in diabetic neuropathy. [*Bibliography: Malik RA, Veves A, Walker D, et al.. Acta Neuropathol. 2001 Apr;101(4):367-74.*]. In our study, the compression accelerated the progression of diabetic neuropathy, the MNCV declined at 2 weeks after compression. Also the pathological morphologic quantification of myelinated fiber was used in many researches as a conventional quantitative methods. So we considered the put the emphasis on test of myelinated fibers. It also may be enough to testify the results of SWE. Based on your valuable advice, we have added some contents in discussion (Please see **Page12, line649-652**) and conclusion (Please see **Page14, line 818-819**), also we add two bibliography mentioned before in paper, **numbered 32, 33**.