THE EARLY CHANGES IN AXONAL PROPERTIES IN PREDIABETES

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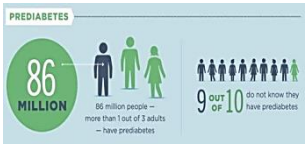
Background

The neurologic complications of diabetes may arise as early as prediabetes. The possible mechanisms of prediabetic neuropathies are prolonged hyperglycemia, microvascular insufficiency. Previous study showed nerve injury and glucose metabolism in prediabetes may transiently improve in the 1st year after diet control and exercise.[1] Multifactorial intervention such as control of hypertension, dyslipidemia and smoking cessation are effective for neuropathies.[2] To detect early changes in prediabetes is an important task for future prevention of irreversible neurological changes.



Resource: www.cdc.gov/diabetes/prevention

Purpose

In early diabetes, sensory excitability parameters have shown significant changes prior to motor axons[4] more importantly these changes can be detected in patients without neuropathy. The purpose of our study is to evaluate whether these axonal properties already begin to change in prediabetes stage.

Method

53 patients (Table 1) diagnosed as prediabetes were enrolled to receive the nerve excitability test. Prediabetes is defined by American diabetes association (ADA) as one of the three following criterion: HbAIC 5.7% to 6.4%, or fasting glucose 100mg/dL to 125mg/dL, or 2 hour oral glucose tolerance test 140 to 199mg/dL. Age-matched healthy subjects were also received nerve excitability test. Subjects with **radiculopathy**, **myelopathy**, **entrapment neuropathy** such as carpel tunnel syndrome and **polyneuropathy** were excluded. The clinical evaluation includes serum creatinine, lipid profile, nerve conduction study, and nerve excitability measurements All heathy subjects and prediabetic patients also received clinical evaluation including total neuropathy score (TNS).

	Prediabetes (n=53) Mean (SD)	Healthy control (n=22) Mean (SD)	*P* value
Male/female	22/31	11/11	0.751
Age (year)	61.6 (8.9)	62.5 (10.8)	0.706
Temperature	34.5 (1.07)	34.9 (1.55)	0.252
HbA_{1C} (%)	5.86 (0.22)	5.29 (0.28)	<0.001*
Sural nerve amplitude(μV)	13.75 (6.5)	11.37 (4.5)	0.145

Table 1 *Demographic and clinical profile of prediabetes and healthy control subjects*
There is no difference in demographic and clinical features between prediabetes and healthy control subjects.

Results

All patients enrolled in our study with prediabetes have no clinical symptoms and signs nor evidence of diabetic neuropathy. The results of sensory and motor nerve conduction studies were normal in both groups. **Superexcitability** parameters significantly increased in prediabetes (Figure 2C, recovery cycle) when compared with healthy controls. There are no significant difference between two groups in other nerve excitability parameters (Fig. 2). The motor nerve excitability properties are similar in prediabetes and healthy controls (Fig. 3)..

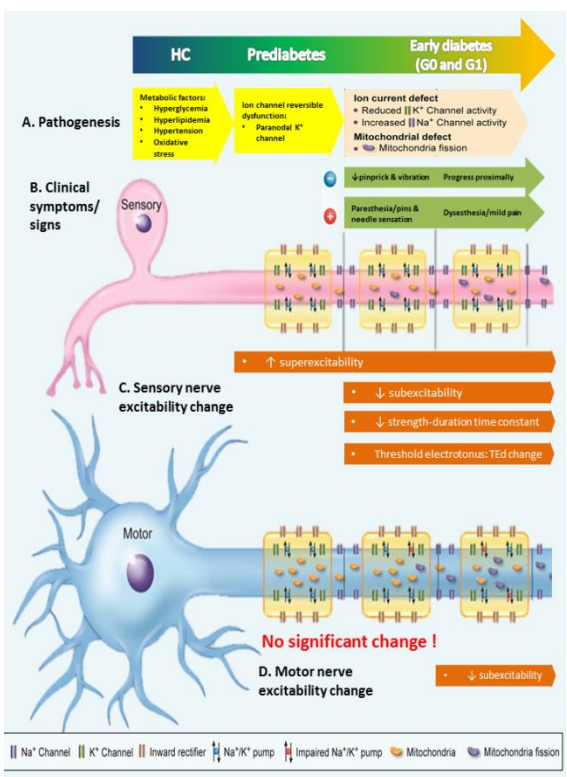


Figure 1: Progression of diabetic neuropathy from pathophysiologic, symptom and signs, and nerve excitability viewpoints. (A) *Pathogenesis of diabetic neuropathy typically progresses from metabolic alteration to ion current defect.* ***(B)*** *Both + /- clinical signs/symptoms* ***(C)*** *Sensory excitability changes occurred early in prediabetes stage.* ***(D)*** *Motor excitability changes can not be detected at prediabetes stage.*

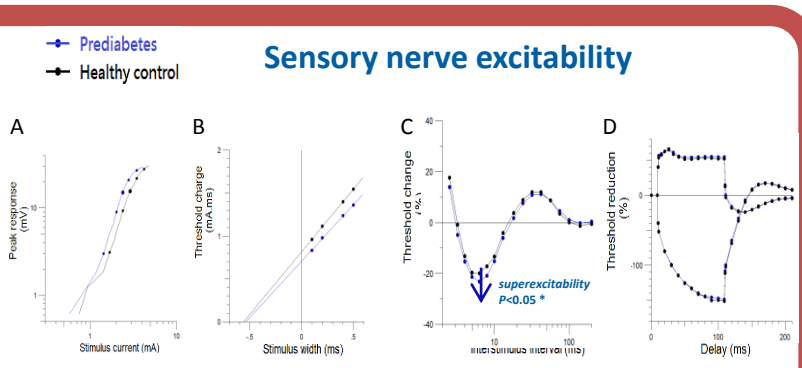


Figure 2: Sensory nerve excitability changes in prediabetes versus healthy control.
(A)Stimulus current : no significant difference between prediabetes and healthy control .
(B) Strength duration properties : no significant difference between two groups.
(C) Recovery Cycle : Superexcitability is significantly increased in prediabetes
(D) Threshold electrotonus: no statistical differences between two groups

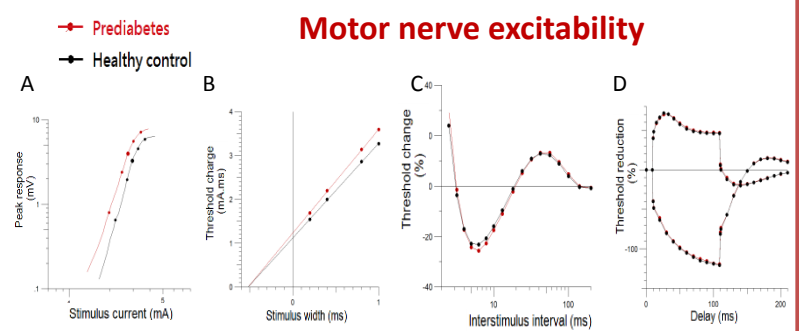


Figure 3: Motor nerve excitability changes in prediabetes versus healthy control.
(A)Stimulus current : no significant difference between prediabetes and healthy control .
(B) Strength duration properties : no significant difference between two groups
(C) Recovery Cycle : no significant differences between two groups
(D) Threshold electrotonus : no significant difference between these two groups

Conclusion

Sensory axons are more vulnerable than motor axons in prediabetes (Fig. 1). The most sensitive excitability parameter is **superexcitability**, which implies **paranodal slow potassium channel** dysfunction. These results can hint us to evaluate the early diagnosis and to prevent progression to diabetic neuropathies.

Reference

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