

Influence of Vitamin B1 on Diabetic Neuropathy - Studies in Streptozotocin- Diabetic Rats -

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Introduction:

Products resulting from glycation and oxidation are increased in diabetic nerves and inhibition of glycation/oxidation improves parameters of experimental diabetic neuropathy. As thiamine or its lipid-soluble phosphorus ester, respectively, can inhibit development of glucose oxidation products, we investigated the effects of oral administration of thiamine and benfotiamine on the development of glucose oxidation products in the nerve and on nerve conduction velocity in streptozotocin-diabetic rats.

Results:

Nerve conduction velocity decreased in diabetic animals (BS 299 mg/dl, HbA1 11.1%) by 10.5% and CML was increased 3.5-fold. Primary prevention with benfotiamine reduced CML to near-normal values (p vs normal group n.s.) and normalised nerve conduction velocity. Both, primary therapy and secondary interventions with thiamine showed no effect.

Material und Methods:

Ninety male Wistar-rats were divided into six different groups (normal control, diabetic control without therapy, inhibition study: after injection of streptozotocin immediate therapy with benfotiamine, inhibition study: after injection of streptozotocin immediate therapy with thiamine, reversibility study: after diabetic interval of two months therapy with benfotiamine, reversibility study: after diabetic interval of two months therapy with thiamine). As metabolic parameters, blood sugar and HbA1 were measured, as functional parameters nerve conduction velocity and neural accumulation of N^ε-(carboxymethyl)-lysine (CML) were assessed. Neural CML accumulation in protein extracts of the n. brachialis was quantitated using a monoclonal CML antibody (kindly provided by Dr. S. Horiuchi, Kumamoto, Japan) and an immunoblot procedure as described (Diabetes 47, 401, 1998)

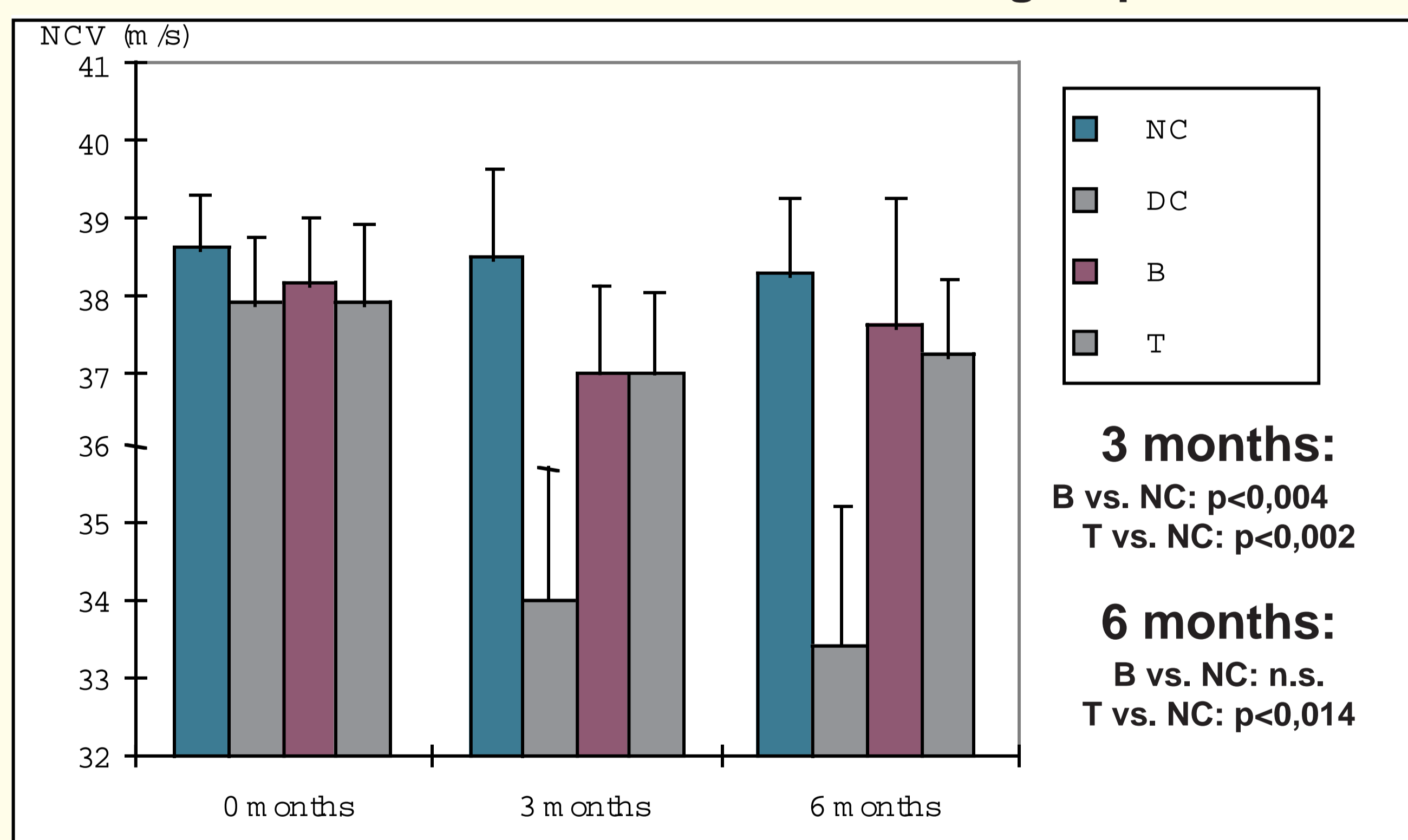
Design: Six groups containing of 15 animals each were randomised

NC	Normal control
DC	Diabetic Control - no treatment
B	Inhibition study - After streptozotocin injection immediate treatment with benfotiamine (100 mg/kg bodyweight)
T	Inhibition study - After streptozotocin injection immediate treatment with thiamine (70.18 mg/kg bodyweight)
B2	Reversibility study - Two months after diabetes induction treatment with benfotiamine (100 mg/kg bodyweight)
T2	Reversibility study - Two months after diabetes induction treatment with thiamine (70.18 mg/kg bodyweight)

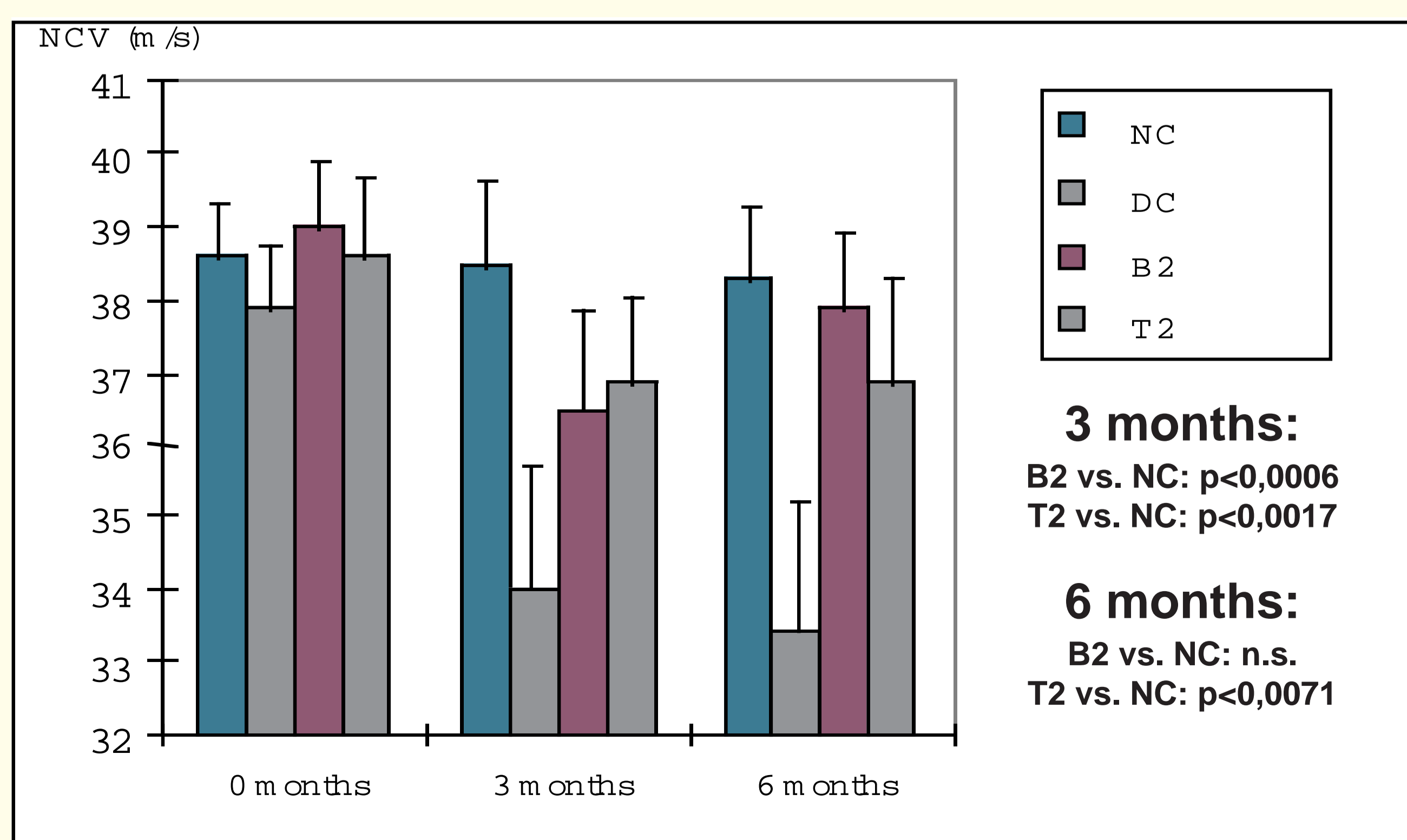
Blood glucose	Basal value	3 months	6 months	D03	D36	D06
Group NC	87.50±5.67	86.50±5.05	100.50±13.39	-1.0±7.4	14.0±11.0	13.0±12.3
Group DC	87.40±15.87	283.8±176.79	299.20±179.92	196.4±162.3	15.4±140.3	211.8±169.1
Group B	86.09±10.82	333.64±112.90	373.36±112.90	247.6±116.6	39.7±62.6	287.3±137.2
Group T	90.08±8.64	341.92±99.68	317.85±123.05	251.9±93.8	-24.1±112.7	222.8±118.0
Group B2	94.33±10.14	377.00±195.44	387.42±161.83	282.7±197.3	10.4±142.2	293.1±164.1
Group T2	100.31±17.18	380.92±152.38	391.62±147.30	280.6±148.1	10.7±150.2	291.3±145.2

HbA1	Basal value	3 months	6 months	D03	D36	D06
Group NC	4.80±0.58	5.07±0.60		0.27±0.50		
Group DC	4.48±0.40	11.09±4.81		6.60±4.82		
Group B	5.02±0.52	13.09±3.57		8.08±3.31		
Group T	4.88±0.44	13.54±4.32		8.67±4.19		
Group B2	5.02±0.30	12.89±4.08		7.87±4.03		
Group T2	5.21±0.68	12.64±3.90		7.43±4.12		

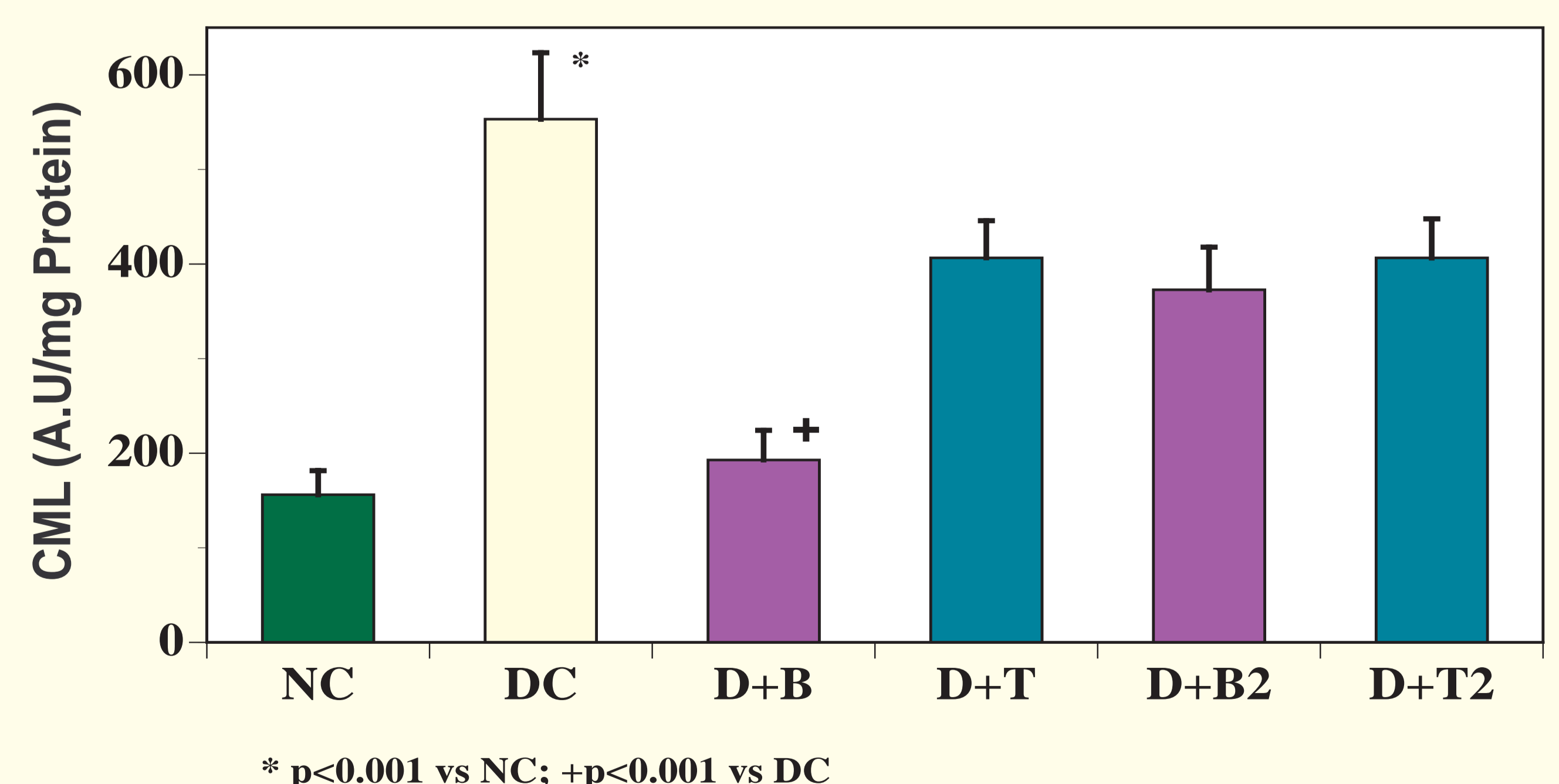
NCV (m/s) inhibition study:
treatment vs. diabetic / normal group



NCV (m/s) reversibility study:
treatment vs. diabetic /normal control



Glycation/Oxidation Products in the Nerve



Conclusion:

Early treatment with benfotiamine normalizes increased cellular oxidative stress and the reduced nerve conduction velocity.