Diabetes Mellitus: Risk or Protective Factor in ALS?

Alicia R Salamone, Michael W Wheaton, Emily J McDowell, Adriana M Strutt and Paul E Schulz
Center for Neurodegenerative Disorders, Department of Neurology, Baylor College of Medicine, Houston, TX

Introduction

Identifying factors that alter the course of degenerative disorders should give a clue as to the pathophysiology underlying them.

Few factors are known to affect the course of amyotrophic lateral sclerosis (ALS). Glucose and insulin dysregulation have been suggested. However, premorbid dysfunction has not been examined for its effect on the presentation and course of ALS.

Methods

Between 1977 and 2006, 2372 consecutive patients were examined at the time of their initial evaluation for ALS.

All patients diagnosed with probable or definite ALS (El Escorial criteria) were included. All were tested for diabetes mellitus (DM). Charts were retrospectively reviewed for disease variables.

Tables 1 and 2. Demographics

	N	Mean	Std. Deviation
Age at First Symptom	2359	56.6	13.3
Rate of Progression (Appel Scale)	651	3.1	2.9
Length of Disease (yrs)	891	3.2	2.3
Education (years)	523	13.8	3.2

	Frequency (N=2372)
Male	62.0%
Caucasian	89.1%
Right-Handed	93.3%
Diabetics	7.4%

Results

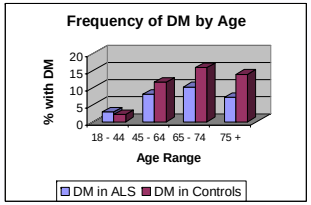

Figure 1. DM is less frequent in the ALS cohort than in age and location-matched controls

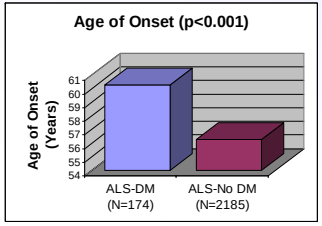

Figure 2. ALS-DM patients have a 4 year later age of onset than do ALS-No DM patients (60.3 vs 56.3)

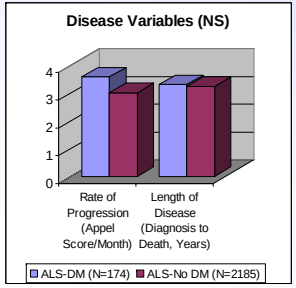

Figure 3. Rate of progression and length of disease of ALS were similar between ALS-DM and ALS-No DM

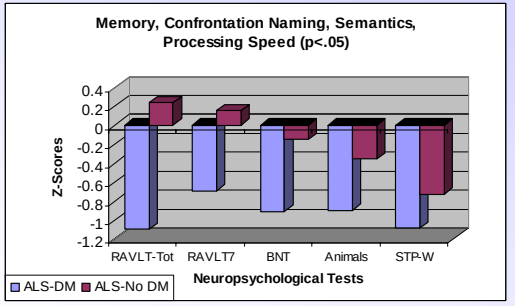

Figure 4. ALS-DM patients performed more poorly on several domains, which tend to be relatively preserved in ALS

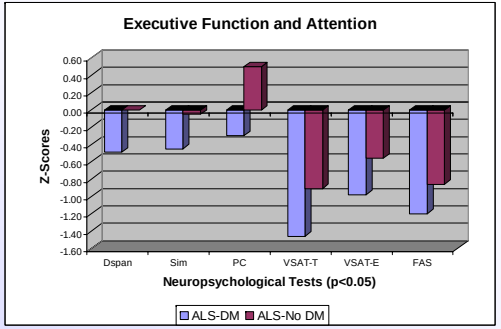

Figure 5. ALS-DM patients scored worse on executive function and attention

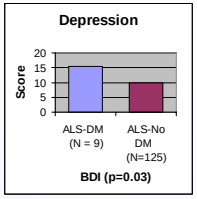

Figure 6. ALS-DM patients were more depressed

Cognitive Status by FAS Score	Percent with DM
Intact (-1 < Z < 1, N=228)	3.1%
Mild (-2 < Z < -1, N=163)	5.5%
Moderate (-3 < Z < -2, N=50)	16.0%

Table 3. Presence of DM is associated with increased severity of cognitive impairment (p=0.001)

Conclusions

Motor

- ALS-DM pts had a 4 year later age of onset for motor symptoms, but did not have a faster progression rate or shorter duration of disease as would be expected.

Cognitive

- ALS-DM pts had worse cognition and depression than non-DM pts
- The pattern of cognitive impairment may *differ* between DM and non-DM pts with DM pts having greater problems with memory, confrontation naming, verbal fluency, and depression. It is not clear, then, whether DM worsens FTD or causes a different kind of cognitive impairment.

To conclude, DM delays the onset of motor symptoms, but is associated with worse cognitive findings.