FUNCTIONAL AND STRUCTURAL ASSESSMENT OF SENSORY NERVE FIBRES IN MOTOR NEURON DISEASE

Baris Isak¹, Kirsten Pugdahl², Pål Karlsson³, Hatice Tankisi⁴, Nanna BrixBinnerup², Jasna Furtula¹, Birger Jøhansen⁵, Niels Sundé, Johannes Jakobsen⁵, Anders Fuglsang-Frederiksen⁵

¹ Department of Clinical Neurophysiology, Aarhus University Hospital, Aarhus, Denmark, ² Danish Pain Research Centre, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark, ³ Department of Neurosurgery, Aarhus University Hospital, Aarhus, Denmark, ⁴ Department of Neurology, Aarhus University Hospital, Aarhus, Denmark

Background:

1. Increasing evidence suggests that ALS is a multisystem disorder involving also sensory nerves.
2. Pathological studies showed the involvement of myelinated sensory nerves in 70–90% and unmyelinated nerves in 79% of ALS patients.
3. Yet, sensory signs are neither the main complaints of an ALS patient nor the major problem of the physician to investigate.

Aim: Functional [i.e. quantitative sensory testing (QST)] and structural (i.e. skin and nerve biopsies) measures were used to assess involvement of sensory nerve fibers in ALS patients.

Methods: Thirty-two ALS patients and 32 controls were enrolled.

1. QST battery (all patients and controls); Thresholds of mechanical detection (MDT), mechanical pain (MPT), vibration detection (VDT), cold detection (CDT), warm detection (WDT), heat pain (HPT), and pinprick sensation.

2. Skin biopsies (31 patients); intraepidermal nerve fiber density (IENFD) (marker of derervation), axonal swelling ratios, and growth-associated protein 43 (GAP-43) antibody staining (marker of re-innervation).

3. Sural nerve biopsies (8 patients); teased fiber analysis.

Statistics: Data from the healthy subjects were used to obtain normative limits. For skin and nerve biopsies reference values obtained from EPINS guidelines and values given by Dyck were used, respectively. Values within mean ± 1.96 SD (cut off) were regarded normal. Statistical analysis was performed using Stata 13 (Stata Corp LP, Texas, USA). Normal distribution was determined based on Q-Q plots and histograms. Data not following a normal distribution were log-transformed. Continuous data were analyzed using student’s t-test for normative data. Categorical data were analyzed using Fisher’s exact test.

Results:

1. Mean values for QST parameters and IENFD in ALS patients were within normal range.
2. Four patients (12.5%) had two or more abnormal QST parameters, while three patients (9.6%) had reduced IENFD.
3. All patients had increased axonal swelling ratios and none of them had GAP-43 antibody stained fibers.

Discussion:

1. Concordant with involvement pattern of sensory fibres in ALS; QST, sural nerve biopsy, and IENFD were affected only in few ALS patients.
2. Axonal swellings observed in all patients indicated a mild but consistent pathological involvement of small nerve fibers.

References:


barisisk@gmail.com