MOTOR UNIT NUMBER INDEX (MUNIX): READY FOR CLINICAL ALS TRIALS – A 15 MONTHS LONGITUDINAL MULTICENTRE TRIAL

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Background: Motor Unit Number Index (MUNIX) is a novel neurophysiological measure that provides an index for the number of motor neurons in a muscle (1, 2) and is an ideal candidate to track lower motor neuron loss in ALS patients.

Objective: To investigate MUNIX in a set of muscles, in ALS patients, in a longitudinal multicentre setting to evaluate its sensitivity as a marker for disease progression in comparison to functional decline, as represented by ALSFRS-R.

Methods: Between 07/2010 and 01/2014 three study centres applied the MUNIX technique in 48 ALS subjects over 15 months. Six muscles (biceps brachii (BB); abductor digiti minimi (ADM); abductor pollicis brevis (APB); tibialis anterior (TA); extensor digitorum brevis (EDB); abductor hallucis (AH)) were measured in each subject on the clinically less affected side of the body, every 3 months. Decline of MUNIX and ALSFRS-R was compared.

Results: MUNIX was easy to perform and well tolerated. Out of 48 patients, 38 reached a follow-up visit at month 12. The muscle-specific intraclass correlation coefficient (ICC) showed very good reproducibility (Intra-rater reliability between 0.81 and 0.97, mean 0.89, Inter-rater reliability 0.46 and 0.92, mean 0.80). The relative decline of MUNIX differed between muscles and was different between subgroups of subjects with bulbar, lower and upper limb onset. For all subjects, ALSFRS-R declined at a rate of 2.3% per month. MUNIX of AH and BB declined at a similar rate (2.4% and 2.6%). Other muscles declined at higher rates between 3.3% and 4.2% and were statistical significant at several points in time (p < 0.05 _ 0.002). Using the total score of MUNIX (either of all 6 or of the 4 muscles excluding AH and BB), MUNIX 6 declined significantly with 3.2% decline per month, and MUNIX 4 with 3.7% per month (p < 0.03 _ 0.0005). Subgroup analysis revealed different rates of decline in ALSFRS-R for bulbar onset subjects (2.8% per month, n = 17) and lower (2.1% per month, n = 15) or upper limb onset (1.9% per month, n = 16), while MUNIX 4 and MUNIX 6 showed similar decline rates across all subgroups (MUNIX 4: 3.6% to 3.8% per month, MUNIX 6: 3.1% to 3.4% per month).
Discussion and conclusion: MUNIX measurements in multiple muscles reveal a
good inter- and intra-rater reliability for detecting decline in ALS subjects.
MUNIX decline significantly exceeded decline of ALSFRS-R in several muscles in
spinal onset ALS subjects and is similar to ALSFRS-R decline in bulbar onset
ALS subjects. While ALSFRS-R decline differs in different onset subgroups,
MUNIX total scores reveal the same decline rates in all subgroups.
Consequently, MUNIX is a reliable electrophysiological biomarker to track the
underlying disease process of lower motor neuron loss in ALS.

**keywords**
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