**OnWebDuals Consortium: Spreading in ALS**

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**Introduction**

We analyzed disease spread in a large consecutive group of ALS patients, recruited in 5 centers (Antalya, Hannover, Jena, Lisbon and Warsaw) and evaluated according to a common protocol. We provide a structured analysis of disease spread by anatomical region and by predominant upper (UMN) versus lower motor neuron (LMN) manifestations.

**Methods**

1163 patients with ALS and progressive muscular atrophy were included. We considered the following regions of onset, as defined by the functional deficit [Cognition (FTD); Bulbar; Cervical; Lumbo-sacral and Thoracic/Respiratory]. Patients with two simultaneous regions of onset or a generalized presentation were also evaluated. Patients were categorized by predominant UMN vs LMN involvement. We evaluated second and third region of involvement, as well as the time interval.

**Results**

The patients presented with the following regions of onset: FTD (n=13); Bulbar (total n=29: predominant UMN n=111 vs LMN, n=137); Cervical (total, n=385: right n=199 versus left arm onset n=138); Lumbosacral (total, n=407: predominant UMN, n=72 vs LMN, n=311); and Thoracic (n=27). 30 patients presented with two simultaneous onset regions and 9 patients had generalized presentation (> 2 regions). Patients with Bulbar-onset progressed preferentially to Cervical (50%) and then to the Lumbosacral region. The latter was not affected by the predominant UMN vs LMN profile, but FTD occurred early more frequently in UMN group. Patients with Cervical-onset progressed preferentially to Lumbosacral (55%) and then to Bulbar region, regardless of side of onset. Patients with Lumbosacral-onset progressed preferentially to Cervical (65%) independently of predominant UMN vs LMN profile. Patients with FTD-onset progressed preferentially to Bulbar region (70%) and then to Cervical region.

**Discussion**

In our study, disease spread seemed more determined by motor neuronal proximity in spinal cord-brain stem than by UMN dysfunction. There was an association between FTD and UMN bulbar involvement.