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Disease burden in upper motor neuron syndromes: a survey of patient perspectives

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Upper motor neuron (UMN) syndromes are a group of degenerative neurological disorders that are classified as either hereditary spastic paraplegia (HSP) or primary lateral sclerosis (PLS) based on phenotypic and genetic characteristics. HSP comprises a group of inherited diseases that are typically characterized by progressive spasticity of the legs[1]. PLS is a disorder of the UMNs that usually begins in the legs, but can begin in the upper body or bulbar muscles[2]. Regardless of the site of onset, UMN dysfunction eventually progresses to affect all muscles, differentiating this condition from HSP. Both syndromes are rare, progressive disorders with no known cure.

Here, we report the results of an online survey among individuals registered with the Spastic Paraplegia Foundation (SPF), a non-profit organization dedicated to raising awareness and promoting research for UMN syndromes. The goal of the survey was to gain a better understanding of patients' perspectives with regards to disease burden. The survey was posted on the SPF website and an invitation to participate in the survey was sent by email to all individuals registered with the SPF. Two-hundred twenty-one people responded to the survey. Fifty-six percent of responders reported a diagnosis of HSP (N=124) and 32% a diagnosis of PLS (N=72). The remaining 12% had either ALS or did not have a clear diagnosis. Only responses from people with HSP and PLS were further analyzed. Among

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respondents with HSP, mean age was 54 (± 13 years) and mean disease duration from time when patient first noticed symptoms was 20 years (± 14). Among patients with PLS, mean age was 61 (± 10 years) and mean disease duration from time when patient first noticed symptoms was 14 years (± 8). The four most common symptoms included spasticity, stiffness, loss of balance, and difficulty walking (all present in at least 80% of responders). Fatigue, pain and difficulty with bladder control were present in at least 40% of responders. Depression and sleep problems were present in a third of responders. PLS patients reported additional symptoms related to bulbar dysfunction (difficulty speaking 71%, difficulty swallowing 46%, increased saliva 43%) and pseudobulbar affect (42%). Difficulty walking was reported as the most bothersome symptom by both HSP and PLS patients (Figure 1). The vast majority of patients were using at least one mobility device (86% of HSP patients, 92% of PLS patients). Most patients (88%) used at least one medication to treat spasticity and/or pain with a third of patients using at least two medications.

This study provides a patient-centered description of the most common and relevant symptoms for people with upper motor neuron syndromes. Disease burden included high prevalence of spasticity, stiffness, loss of balance, and difficulty walking, with the latter being reported as the most bothersome symptom. A crucial question that is often asked by researchers, clinicians, and regulatory agencies is what features of the disease are most important to affected individuals. Knowledge about the most bothersome symptoms provides the base data necessary to develop disease-specific, patient-relevant outcome measures to use in clinical trials. Interestingly, the Food and Drug Administration (FDA) has established patient-centered, patient-validated, and patient-reported metrics as part of its criteria for drug approval and labeling[3]. Further, the increasing focus on patient-centered health care is reflected by initiatives such as the establishment of the Patient-Centered Outcomes Research Institute (PCORI). Based on the results of this survey, interventions aimed at improving walking, either pharmacologically or through rehabilitation, are likely to make a significant impact on disease burden and improve quality of life. Difficulty speaking was the second most bothersome symptom for people with PLS, while spasticity, stiffness, and pain were reported as bothersome by both PLS and HSP patients. Thus, outcomes related to these symptoms should ideally be included when designing interventional trials for these patient populations.

This study has several limitations. Although the registry represents a wide range of ages and geographic locations, this sample does not fully represent the HSP / PLS population. In addition, the survey was a voluntary online tool. Not every eligible patient on the registry completed it. Therefore, there is the potential for sampling bias that could affect the generalizability of our results. Survey responders probably over-represented individuals who are interested in medical research and have the physical function necessary to access a computer and take part in research.

Nevertheless, this study is, to the best of our knowledge, the largest patient-centered survey conducted among people with rare upper motor neuron syndromes. These findings can help enable clinicians and researchers to focus on the manifestations and management issues that are most important to those affected by HSP and PLS.

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Abbreviations

FDA	Food and Drug Administration
HSP	hereditary spastic paraplegia
PCORI	Patient-Centered Outcomes Research Institute
PLS	primary lateral sclerosis
SPF	Spastic Paraplegia Foundation
UMN	Upper motor neuron

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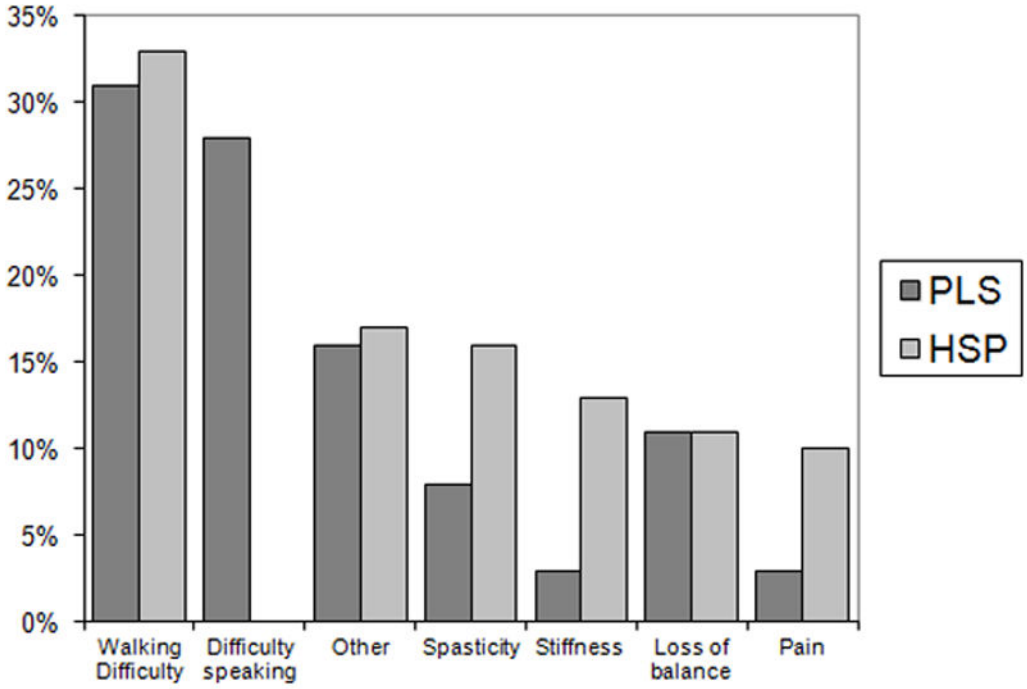

Figure 1.
Most bothersome symptom in PLS and HSP patients.