

Full Title: Analysis of the terms used for the diagnosis and classification of amyotrophic lateral sclerosis and motor neuron disease

Running title: Analysis of terms used for amyotrophic lateral sclerosis

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Abstract

There is no test for amyotrophic lateral sclerosis (ALS) and so attempts have been made to produce standardised diagnostic criteria based on clinical and electrophysiological findings. The phenotypic classification of the subtypes of ALS is also based on clinical features, which leads to conflation of diagnosis and phenotype. We gave a five question online survey to ALS specialists to explore the range of descriptors and their use. Of 101 specialists approached, 72 completed the survey. The most frequently used labels were 'ALS', 'PLS' and 'familial'. Labels other than the El Escorial categories were mainly used as clinical descriptors (83%). Approximately 50% of respondents recorded that the El Escorial Criteria had no useful role in patient discussion or in the diagnostic process. Only 31% of respondents rated their current classification system above the median for being logical. A more rational system explicitly distinguishing diagnostic and phenotypic criteria is essential.

Keywords:

Classification of ALS/MND

Diagnosis of ALS/MND

Phenotype of ALS/MND

Introduction

Amyotrophic lateral sclerosis (ALS) was first described by Charcot as characterised by the pathological combined degeneration of upper and lower motor neurons. More recently ALS has been recognised as a syndrome, clinically and pathologically overlapping with frontotemporal dementia. There is no test for ALS and as a result, the diagnosis is based on clinical assessment by an experienced neurologist. The phenotype of ALS is also based on clinical features, with a wide range of descriptive terms for both ALS and its variable clinical presentations.

Before a more rational approach to diagnosis and classification is possible it is important to appreciate the breadth of terms currently in use. We therefore surveyed ALS specialists to test the hypothesis that an inconsistent set of terms is in widespread use, to explore their frequency, and understand the breadth and use of descriptors.

Methods

A five question survey was designed using open access online software (SurveyMonkey®) and piloted on four UK-based ALS specialists. Specialist ALS clinicians were emailed an invitation to participate in the full survey, with a link (<https://www.surveymonkey.com/s/3N22NFJ>) embedded in the email (Figure 1).

Statistical tests were carried out using Microsoft Excel (Microsoft Corporation, USA) and SPSS (SPSS Inc, Illinois, USA). The Fisher exact test was used to calculate differences in responses by continent. For analysis, Australia was grouped with Europe, and Canada with the USA (North America group).

Results

Of 101 clinicians approached, 72 completed the survey (71%). Every option was used by at least one respondent (Figure 2). The most frequently used labels were ‘ALS’, ‘PLS’ and ‘familial’ and the least used were ‘slowly progressive motor neuropathy’, ‘corticobulbar palsy’ and ‘Charcot ALS’.

Labels based on degree of upper and lower motor neuronal involvement were used by 67 (93%) respondents, labels based on burden of weakness by 56 (78%), labels based on neuroanatomical segment involved at first symptoms by 47 (65%), and labels based on family history by 58 (81%). 30 (42%) respondents used one or more of the versions of El Escorial criteria: 12 using the original El Escorial criteria, 13 the Airlie House revision, and 17 the Awaji revision.

There were 22 respondents from the North America group and 44 from the Europe group. The 6 most frequently used terms were of similar frequency in the two groups (Figure 3).

Labels other than the El Escorial categories were mainly used as clinical descriptors (59 respondents, 83%) (Figure 4a).

More than 50% of respondents said that the El Escorial Criteria had no useful role in any patient discussion or in the diagnostic process, with the remainder split unevenly between using the Criteria for diagnosis (26%), clinical classification (26%) and patient communication (15%) (Figure 4b).

Respondents rated their current classification system from 1 (completely illogical) to 10 (completely logical), with a median response of 7 (Figure 5). There was no difference by continental grouping. Only 21/68 rated their current classification system above the median for being logical.

Most respondents (62, 92.5%) did not record disease stage using any system.

Discussion

We have confirmed that a large number of terms are used for the diagnosis and clinical description of ALS, with no significant differences between European/Australian and North American practice. The descriptors used cover multiple domains, many of which are not consistent, and this is reflected in the rating of the classifications used as only partly logical. Use of clinical staging systems is not yet part of usual practice.

A consistent and rational approach to the diagnosis and phenotypic classification of adult motor neuron diseases is needed. The development of an *in vivo* diagnostic test may help, but in the meantime, a system explicitly distinguishing between rules for diagnosis and rules for the description of phenotype is essential. Furthermore, any classification system should take into account that observed parameters are continuous variables and there are no objective cut-offs. As a first contribution to this debate, we suggest an approach using two tiers. The first tier includes ALS and PLS, and the second tier more detailed descriptive terms such as ALS upper motor neuron predominant, ALS-lower motor neuron predominant, ALS-FTD, ALS-Flail Arm, ALS-Flail Leg, ALS-PMA, and potentially other phenotypes. We have to bear in mind that these patterns change during the evolution of the disease, so ultimately any descriptors should be linked to disease stage (e.g., ALS-Flail Leg/Stage 3). Although there is scope for debate, a classification system explicitly separating diagnosis and phenotype, and recognising that phenotypic features evolve, will provide more clarity to clinicians, patients and academics.

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FIGURES

Figure 1. The survey sent to clinicians specialising in ALS

Figure 2. Frequency of survey responses.

Figure 3. Descriptors used broken down by place of practice

Red = Europe and Australia, Blue = USA and Canada

Figure 4a. Use of clinical descriptors excluding El Escorial criteria

Figure 4b. Use of El Escorial criteria

Figure 5. Respondents rated their current system as largely illogical.

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