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Short communication

Classification of dystonia in childhood

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ABSTRACT

Objective: The most recent international consensus update on dystonia classification proposed a system based on 2 axes, clinical characteristics and aetiology. We aimed to apply this system to Children and Young People (CAYP) selected for movement disorder surgery, and determine if meaningful groupings of cases could be extracted.
Methods: The 2013 Consensus Committee classification system for dystonia was retrospectively applied to 145 CAYP with dystonic movement disorders. Two-step cluster analysis was applied to the resulting categorisations to identify groupings of CAYP with similar characteristics.
Results: Classification resulted in a total of 43 unique groupings of categorisation. Cluster analysis detected 4 main clusters of CAYP, comparable to previously used patient groupings.
Conclusions: The 2013 consensus update on dystonia classification can be applied to CAYP with dystonia. The large number of categories provides a wealth of information for the clinician, and also facilitates data driven grouping into clinically meaningful subgroups.

1. Introduction

Dystonia is a common presentation in paediatric practice, differing from that seen in adult practice [1,2], arising frequently as a symptomatic condition [3,4], often found coincident with spasticity [1,4] and with a motor phenotype expressed upon the back ground of ongoing brain development [2]. A number of definitions for dystonia have been proposed, most pertinent to paediatric practice being the definition of the Taskforce for Childhood Motor disorders, reported in 2003 [5]. Almost 10 years after these definitions were proposed, a Consensus Committee established under the auspices of the Dystonia Medical Research Foundation, the Dystonia Coalition and the European Dystonia Cooperation and Technology published an updated definition for dystonia in 2013 [6]. "*Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both. Dystonic movements are typically patterned, twisting, and may be tremulous. Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation*".

Accompanying this revised definition is a classification system along two axes 1) Clinical Characteristics and 2) Aetiology. A combination of the descriptors on the two axes was considered to *"provide meaningful information on any dystonia patient and serve as a basis for the development of research and treatment strategies"*. This revised classification has potential benefits over those previously proposed, not least of which being the move away from the overly reductive division into "primary" and "secondary" dystonia, with the attendant difficulties these terms have posed [6]. One potential benefit is also to facilitate syndromic associations, aiding recognition of distinct disease entities, ultimately aiding diagnosis.

We aimed to determine whether the proposed classification system could:

- Be applied to a consecutive cohort of children and young people (CAYP) undergoing Deep Brain Stimulation (DBS) surgery
- Provide meaningful grouping and subgroupings across this cohort from which to extract prognostic information

Following classification of 145 CAYP, a two-step cluster analysis was used to determine if clinically relevant sub-groupings could be identified across categorized subjects.

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2. Methods

From the Complex Motor Disorder Service Database, a cohort of CAYP were identified who had passed through the full assessment process for DBS surgery at our centre between July 2005 and January 2015 and had been considered suitable for surgery. The clinical notes of all CAYP identified were reviewed, and a standardized data pro-forma used to record data from each subcategory of the revised classification system. Classification was performed from data available at the point of baseline prior to potential surgery. Because the study was a retrospective audit of routine clinical practice, ethics approval was not required and consent was neither required nor obtained.

3. Statistical analysis

Two-step cluster analysis was performed using SPSS Version 22 (IBM, Armonk, New York, USA). Categorical data for the subcategories of the revised classification system was used to identify clusters of CAYP with similar dystonia characteristics. Clustering was achieved by a clustering feature tree, based on an agglomerative clustering algorithm. Selection of optimal clustering was achieved using Schwarz's Bayesian criterion. The quality of fit of the resultant modeled clusters was measured using the Silhouette measure of cohesion and separation. Data from "Body Distribution" and "Temporal Pattern – Variability" were excluded from analysis as almost all CAYP presented with generalized dystonia, and in all cases dystonia was persistent.

4. Results

Classification was possible for all 145 CAYP, resulting in 43 unique groupings of categories. The largest unique grouping consisted of 37 cases. These CAYP were classified as generalized dystonia with leg involvement, static course, persistent dystonic symptoms, combined dystonia, evidence of structural lesions on neuroimaging and acquired aetiology with onset <2 years. Subjects within this group all met the diagnostic criteria for Cerebral Palsy. The next largest grouping consisted of 8 CAYP. A total of 20 unique groupings included just one CAYP.

2 step-cluster analysis suggested separation into 4 main clusters from these 43 unique groupings. The silhouette measure of cohesion and separation of 0.5 suggested a "fair" to "good" cluster segregation. The predominant characteristics of the clusters identified are outlined in Fig. 1 and Table 1.

5. Discussion

For a cohort of CAYP with dystonic movement disorders selected for DBS surgery we have demonstrated: i) application of the most recently proposed dystonia classification system is possible, and ii) the system provides the means by which to generate clinically meaningful groupings in addition to providing richness of data at the individual level.

Classification systems for disease entities must necessarily evolve over time, as an understanding of underlying disease processes and prognostic factors for outcome grow. Dystonia classification has passed through numerous iterations following the initial groupings proposed by Fahn and Eldridge in 1976 [7]. This original system introduced a system based on aetiology, with dystonia divided in "Primary", "Secondary" or "Psychogenic". Over time it has become recognized that the precise application of these classifications was troublesome, as outlined by Albanese and Colleagues in their Consensus Update [6].

The two-axis approach of the Consensus Update provides a clinical richness to the classification of dystonia previously lacking. Axis 1 and Axis 2 are sub-divided into 6 and 3 independent subcategories respectively. Considering the sub-options within each of these categories (and leaving aside the listing of associated neurological features) > 20000 possible independent sub-category combinations may be generated. In practice, not all of these groupings are clinically plausible (e.g. a perinatal brain injury giving rise to a paroxysmal dystonia in late adulthood). Reducing this vast range of options to a more practical number for the purposes of comparative work and prognostication is a necessity. Across a cohort of 145 CAYP we identified 43 independent unique classifications, reflective of the broad range of clinical syndromes giving rise to dystonia in childhood (only 64/145 CAYP presenting with isolated dystonia). From this large range of grouping, an independently driven cluster analysis was able to identified 4 subgroupings. In our previous reported we have pragmatically grouped CAYP with dystonia into categories of "Primary/Primary-plus", "Secondary-Static" and "Secondary-Progressive" [8,9].

Remarkably, these categorisations closely resemble the clusters resulting from our present analysis, Cluster 1 comparable to our Primary/Primary-Plus group, Cluster 2 our Secondary-Progressive (AKA heredo-degenerative) group and Clusters 3 and 4 resembling the Secondary-Static dystonia groupings (Cluster 3 due to CP, Cluster 4 due to other causes). Cluster analysis methods provide data driven techniques for identifying subjects across data sets with similar characteristics. Our present analysis provides some degree of validation both for our choice of these classifications in our previous reports, and for the utility of the Consensus Update Classification itself. This validation is, however, limited by the population upon which the classification has been applied. As only cases within the paediatric age range have been included, caution must be taken in extrapolating our findings across more adult populations. Further validation of the Consensus Update Classification within the adult population is still required, as well as in a less highly specialist paediatric sampling.

Early onset-dystonias present specific challenges for classification. Children may present early in their disease course, prior to the evolution of all clinical/radiological features. Children with DYT1 dystonia will typically present with a focal dystonia, before generalization of dystonic symptoms over a variable time period, changing the pattern of anatomical classification. Similarly, for these children dystonic symptoms will appear to be progressive during the early stages of the disease course, before reaching a stable/static phase. Neuroimaging performed early in the disease course for neurodegenerative disorders (e.g. Neuronal degeneration with brain iron accumulation) may not yet demonstrate characteristic abnormalities. Categorisation of individual CAYP may change over time, and should be considered a dynamic process rather then a static label. Our presented study has not examined the stability of classification over time, and further work is required to explore how frequently the classification of a given child should be revisited, potentially an important consideration for studies of the natural history of this patient population.

One limitation of the Consensus classification system is the lack of information regarding functional status of subjects. We believe that this information is imperative when evaluating interventions such as DBS. We have recently demonstrated the relationship between a number of functional scales commonly used in children with CP and the Burke-Fahn-Marsden-Dystonia rating scale across a heterogenous cohort of children with hyperkinetic movement disorders [10]. These scales provide interrelated but complementary information and we would encourage their adoption when reporting the evaluation of subjects with dystonia.

It has been argued that primary dystonia remains a valuable clinico-etiological construct to guide clinical decision making with