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Common data elements and minimum data sets in cerebral palsy: Start small to grow big

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Common data elements (CDE) are precisely defined key words or items in clinical research to allow for a standardized collection of data across multiple sites. Mandatory items of the CDEs are considered as a minimum data set (MDS). The article by Wilson et al.[1] presents the results of an online Delphi survey carried out to establish CDEs and a MDS with the aim to standardize and harmonize phenotypic data in view of further genomic studies in cerebral palsy (CP). Therefore, this is a preliminary step to establish phenotype–genotype and maybe even phenotype–epigenotype correlations based on multiple federated cohorts of individuals with CP. Indeed, genetic, genomic, and epigenomic studies have recently made very good progress in this field.

At the end of this substantial multidisciplinary and international survey, the participants selected 10 items out of 107 as 'mandatory'. At first sight, this seems insufficient to ensure that this MDS could really help enhance deeper phenotyping and further our understanding of the causes and risk factors of a condition as complex as CP. All the more so as half of these items are only administrative data rather than clinical data.

The definition of CP has evolved over time. By relying more on function than anatomical or aetiological impairment, it now includes medical and social parameters that occur in the context of a prenatal or perinatal non-progressive brain injury.[2] As such, and despite a rather small proportion of individuals with CP having an underlying monogenic cause, researchers and practitioners are calling for CP to be viewed as a clinical entity independently of the underlying cause.[3] This reasonable approach focuses on clinical management that currently does not differ significantly between individuals. The same approach is used in other complex disorders, such as autism spectrum disorders, arthrogryposis multiplex congenita, or congenital myopathies. Fortunately, this approach does not exclude the possibility to apply other types of classification according to hypothesis-driven questions in the field.[4] Furthermore, we learned from neuromuscular diseases that going deeper into genetics does not necessarily lead to better understanding but rather higher complexity.[5]

Therefore, at second sight, the relatively small number of items selected for the MDS for CP is highly relevant to (1) ensure that many contributors can collect these items without missing data and (2) help better stratify and classify CP on a higher hierarchical level than aetiology or genetics alone. This approach most probably will open access to CP as a concept to a broader medical community including clinical geneticists. Since some of these patients have overlapping clinical features but distinct classifications, the MDS may represent a unique opportunity to create overarching

This commentary is on the original article by Wilson et al. on pages 1470–1476 of this issue.

interactions between caregivers involved in the management and diagnosis of these patients but working in different networks. From a clinical perspective, this is also a first step towards personalized medicine in the treatment, prognosis, and genetic counselling of these individuals and families. Above all, if the MDS and by extension the CDE for CP could help patients being guided towards the right diagnostic and treatment networks with the relevant keywords for diagnosis between the medical specialties they depend on, this work will likely be a success.

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Stem cell therapy for cerebral palsy: Proceeding with caution

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The young human brain is highly plastic and thus early brain lesions can lead to aberrant development of connectivity and mapping of functions. This is why cerebral palsy (CP) involves a progressive evolution of a movement disorder with age. Thus it is imperative that interventions to treat CP should be initiated as soon as possible in order to restore the nervous system to the correct developmental trajectory.[1] As infants come with an accessible supply of stem cells, i.e. the umbilical cord, it has been mooted for at least 20 years that autologous grafting of such cells could theoretically replace missing neural cell types. Preclinical experiments in animal models have subsequently provided evidence that this may be over-optimistic. Nevertheless such grafts could act indirectly by supplying trophic support for regeneration or modulating inflammatory responses to hypoxia/ischaemia[2] and could be effective when delivered intravenously or intraarterially rather than intrathecally or intracranially.

On the back of such evidence, there has been a gradual move to initiating clinical trials for cord-derived stem cell treatments for CP (alongside less regulated treatments offered by stem cell therapy clinics). According to a recent meta-analysis, randomized control clinical trials have demonstrated that stem cell therapy for CP compared with symptomatic standard care only show a small but significant positive effect on gross motor function. No safety concerns, at least in the short term, have been detected with the reporting of serious adverse events rare and equally distributed among both intervention and control groups.[3] The open label, randomized trial conducted by of Sun et al.[4] adds incrementally to this body of knowledge but nevertheless makes some important contributions. Their previous study had demonstrated that high doses of autologous cord blood cells were more effective than low doses or placebo.[5] Having high doses of cord blood cells available when needed might be more easily achieved by combining multiple allogenic donor cells from either cord blood or stromal-derived mesenchymal cells. There is a theoretical basis to this, as it has been established that mesenchymal stem cells in particular have a low immunogenicity, and can be safely transplanted. Thus the present study[4] has demonstrated that high or repeated dose allogenic grafts delivered intravenously are safely tolerated. Furthermore, for at least one treatment regime, greater increases in Gross Motor Function Measure-66 scores were seen compared to untreated children.

The study was carried out in children aged 2 to 5 years and it was speculated that improvements were brought about by increased rates of myelination of surviving axon tracts. Clearly, there is a case for moving forward to a phase 3 randomized, double-blind, placebo-controlled trial. However, in addition, considering the growing body of evidence that this is essentially a very safe approach, I would hope to see trials moving to ever younger ages where the treatment can have more immediate effects on the original injury, preserving cells, axons, and the developmental environment, thus allowing nervous system maturation to proceed to a more optimal outcome.

DATA AVAILABILITY STATEMENT

Not required.

This commentary is on the original article by Sun et al. on pages 1477–1486 of this issue.