Spasticity, dyskinesia and ataxia in cerebral palsy

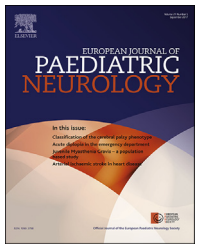
Eggink, H.; Kremer, D.; Brouwer, O. F.; Contarino, M. F.; van Egmond, M. E.; Elema, A.; Folmer, K.; van Hoorn, J. F.; van de Pol, L. A.; Roelfsema, Vincent

Published in:
European Journal of Paediatric Neurology

DOI:
10.1016/j.ejpn.2017.04.1333

Publication date:
2017

Official Journal of the European Paediatric Neurology Society



Original article

Spasticity, dyskinesia and ataxia in cerebral palsy: Are we sure we can differentiate them?

H. Eggink [a], D. Kremer [a], O.F. Brouwer [a], M.F. Contarino [b,c], M.E. van Egmond [a,d], A. Elema [e], K. Folmer [f], J.F. van Hoorn [e], L.A. van de Pol [g], V. Roelfsema [a], M.A.J. Tijssen [a,*]

[a] University of Groningen, University Medical Center Groningen, Department of Neurology, Groningen, The Netherlands
[b] Haga Teaching Hospital, Department of Neurology, The Hague, The Netherlands
[c] Leiden University Medical Center, Department of Neurology, Leiden, The Netherlands
[d] Ommelander Ziekenhuis Groningen, Department of Neurology, Delfzijl and Winschoten, The Netherlands
[e] University of Groningen, University Medical Center Groningen, Department of Rehabilitation Medicine, Center for Rehabilitation, Groningen, The Netherlands
[f] Department of Rehabilitation, Revalidatiecentrum de Trappenberg, The Netherlands
[g] Department of Child Neurology, VU Medical Center Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 13 September 2016
Received in revised form
17 March 2017
Accepted 23 April 2017

Keywords:
Cerebral palsy
Phenotype
Spasticity
Dystonia
Ataxia

ABSTRACT

Objective: Cerebral palsy (CP) can be classified as spastic, dyskinetic, ataxic or combined. Correct classification is essential for symptom-targeted treatment. This study aimed to investigate agreement among professionals on the phenotype of children with CP based on standardized videos.

Methods: In a prospective, observational pilot study, videos of fifteen CP patients (8 boys, mean age 11 ± 5 y) were rated by three pediatric neurologists, three rehabilitation physicians and three movement disorder specialists. They scored the presence and severity of spasticity, ataxia or dyskinesias/dystonia. Inter- and intraobserver agreement were calculated using Cohen's and Fleiss' kappa.

Results: We found a fair inter-observer ($\kappa = 0.36$) and moderate intra-observer agreement ($\kappa = 0.51$) for the predominant motor symptom. This only slightly differed within the three groups of specialists ($\kappa = 0.33–0.55$).

Conclusion: A large variability in the phenotyping of CP children was detected, not only between but also within clinicians, calling for a discussing on the operational definitions of spasticity, dystonia and ataxia. In addition, the low agreement found in our study questions the reliability of use of videos to measure intervention outcomes, such as deep brain stimulation in dystonic CP. Future studies should include functional domains to assess the true impact of management options in this highly challenging patient population.

* *Corresponding author*. University of Groningen, University Medical Center Groningen. Department of Neurology, Hanzeplein 1, 9700 RB Groningen, The Netherlands. Fax: +31 50 3611707.
E-mail address: m.a.j.de.koning-tijssen@umcg.nl (M.A.J. Tijssen).

http://dx.doi.org/10.1016/j.ejpn.2017.04.1333
1090-3798/

1. Introduction

Cerebral palsy (CP) is commonest motor disorder in children.[1] In clinical practice, CP patients are clinically subdivided according to the predominant motor disorder, e.g. spastic, dyskinetic/dystonic or ataxic. Spasticity is defined as hypertonia where 1) resistance to externally imposed movement increases with increasing speed of stretch and varies with the movement direction and/or 2) resistance to externally imposed movement rises rapidly above a threshold speed or joint angle.[1,2] Dyskinesia or dystonia is a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both.[2] Ataxia is characterized by an impairment of the coordination of goal-directed movements, resulting in gait and trunk disturbances, intention tremor and slurred speech.[3]

Spasticity is the most prevalent form of CP, but dystonic CP is the most common cause of childhood dystonia.[1] Moreover, dystonia may be under-recognized and classified as spasticity in children with CP.[4] Accurate phenotyping is of great importance as management is entirely symptomatic and it is becoming increasingly clear that the different phenotypical subtypes require a specific approach.[4] For instance, (intrathecal) baclofen has been proven effective in spasticity whereas deep brain stimulation (DBS) may ameliorate dystonic symptoms.[5,6] Especially in dystonic CP, intervention studies for dystonic CP primarily use video assessments to measure the extent of dystonia, for instance after DBS treatment.[7] The ability to differentiate between spasticity, dystonia/dyskinesia and ataxia in CP is thus essential to reliably phenotype and follow-up of patients.

This pilot study aimed to determine the agreement on the phenotypical classification of children with CP based on video assessment among and within different clinicians working regularly with young patients with CP.

2. Methods

2.1. Patients

This study was approved by the medical ethical committee of the University Medical Center Groningen (UMCG; the Netherlands – M14.164690). We selected fifteen young CP patients who attended the pediatric rehabilitation outpatient clinic of the UMCG. Informed consent or third party assent was obtained in all participants and/or caregivers.

2.2. Assessment

We videotaped the children according to a standardized video protocol of 5–7 min according to a standard neurological examination, including sitting, standing and walking, and examination of muscle tone, deep tendon reflexes, coordination tasks and simple motor tests.

2.3. Clinicians

Nine clinicians regularly working with young patients with CP participated in this pilot study. The clinicians were selected based upon their background (three pediatric neurologists, three pediatric rehabilitation physicians and three neurologists with an expertise in movement disorders) and worked at different institutions all over the Netherlands. Clinicians were carefully selected to enable a fair comparison between the three disciplines. Firstly, all clinicians spend at least six months to one year of their neurology or rehabilitation training in the pediatric department. Secondly, all nine work with pediatric patients in their daily practice. The pediatric neurologists and rehabilitation physicians only work with children and young adults, and the movement disorder experts work with pediatric as well as adult patients. Every group consisted of one experienced clinician (>15 years of post-training experience) and two younger experts (≤10 years of post-training experience). Together they had a mean of 9.8 years (range 2–29) professional experience in their field.

2.4. Phenotypic classification

The nine clinicians were asked to independently classify the CP symptoms of the fifteen patients based on the videotaped assessment. Except from the videos, no other clinical information was provided. To indicate the phenotype, the assessors divided a total of 100 points between the three motor symptoms, i.e. spasticity, dyskinesia and ataxia. For example, a patient could be classified as 40% spasticity, 60% dyskinesia/dystonia and 0% ataxia. Secondly, clinicians were asked localize the described symptoms in seven different body regions (head, neck, trunk, right arm, left arm, right leg, left leg). Thirdly, overall severity per symptom was indicated, using the global clinical impression (GCI) scale ranging from 1 (symptom absent) to 7 (among the most severe spectrum). After a three months interval, eight randomly selected videos were rated again by the nine clinicians.

We determined the inter- and intra-observer agreement on the predominant symptom, defined as the symptom with the highest percentage, for the whole group and the three subgroups (pediatric neurologists, rehabilitation physicians and movement disorder specialists).

2.5. Statistical analysis

The results were analyzed using descriptive statistics, percentage agreement and Fleiss' kappa and Cohen's kappa for inter- and intra-observer agreement respectively. When describing the results, the common description as provided by Landis and Koch was used: $\kappa < 0.2$ for slight agreement, $\kappa = 0.2–0.4$ for fair agreement, $\kappa = 0.4–0.6$ for moderate agreement, $\kappa = 0.6–0.8$ for strong agreement and $\kappa > 0.8$ for almost perfect agreement.[8]

3. Results

3.1. Patient characteristics

Fifteen children (8 boys, mean age 11.1 y, SD 4.7 y) with an extent of symptoms ranging from gross motor function classification system (GMFCS) 1 (walking without limitations) to 5 (transported in a manual wheelchair) were scored.

3.2. Inter-observer agreement on the main feature

As shown in Table 1, all nine clinicians agreed on the main feature in six out of fifteen videos resulting in a 'fair' overall agreement ($\kappa = 0.36$; 95%-CI 0.28–0.44; $p < 0.001$). The pediatric neurologists showed the highest agreement with consensus in 10/15 patients (moderate agreement). Localization of the symptoms and symptom severity (GCI score) and gross motor functioning (GMFCS) did not influence agreement ($p > 0.05$). Spasticity was most frequently seen as predominant symptom, followed by dyskinesia. Dyskinesia was relatively more often reported by pediatric neurologists compared to rehabilitation physicians and movement disorders experts (42% versus 29% and 33% respectively).

3.3. Intra-observer agreement

Intra-observer agreement on the predominant symptom was 'moderate' ($\kappa = 0.51$; $p < 0.0001$) for the whole group, with the pediatric neurologists showing the highest median agreement (see Table 1). None of the clinicians showed a 100% agreement between two ratings on the eight videos that were assessed twice.

In more detail, re-assessment of the videos led to a different reported main feature at the second rating in 25% (18/72) of the cases. Only in one patient all clinicians reported the same main feature on the first and second assessment of the video, whereas in the other seven cases up to five clinicians disagreed with themselves.

Shifts were predominantly seen between a report of spasticity at the first rating to dyskinesia at the second rating ($n = 8$) or vice versa ($n = 8$). In half of these cases the predominant feature accounted for 50–60% of the total phenotype, meaning it was a mixed phenotype because 40–50% of the total score of 100 was explained by one or two additional so-called secondary symptoms. However, in the other nine shifts, the clinicians reported predominant feature accounted for 70–100% of the phenotype, but still changed to another predominant symptom in the second rating.

4. Discussion

This study aimed to evaluate the agreement on the clinical phenotype of children with CP using standardized video assessments among clinicians involved in the care of CP. We found an only 'fair' inter-observer agreement ($\kappa = 0.36$) and 'moderate' intra-observer agreement ($\kappa = 0.51$) for the identification of the predominant symptom.

One likely explanation for the fair agreement among observers is the moderate agreement within observers found in our study. The observed phenotype seems not only to depend on the clinician, but also varies per assessment by the individual clinician. The highly heterogeneous CP patient population in terms of localization, extent and the presence of multiple symptoms in our study might be partly responsible for the relatively low inter- and intraobserver agreement. Remarkably, despite the fact that phenotypical classification of CP is a broadly used way to classify patients, to our knowledge only one previous study from Sellier and colleagues (2012) focused on the interobserver agreement in this population. They found a high agreement ($\kappa = 0.86$) among clinicians based on video assessments of CP patients.[9] In that study vignettes were given to the raters containing information regarding the children's birth characteristics, early developmental history and description of clinical signs of muscle tone and strength not assessed in the videos. Although there are associations between pregnancy and birth abnormalities and radiological characteristics and the development of specific symptoms, these are far from perfect and may bias the raters.[10] We deliberately chose not to provide any background history in our study and videotaped examination of muscle tone and reflexes to ensure capturing the observers' interpretation of the signs. The low intra- and inter-observer agreement indicate a possible structural problem in the demarcation of the concepts spasticity, dyskinesia and ataxia in CP and clinicians might not speak the same language when it comes to those symptoms.

The use of videos instead of live examination might decrease the confidence of the raters in defining and an additional explanation for the low agreement. Our results suggest that clinicians find it very challenging to distinguish particularly spasticity and dystonia. An accurate classification of the symptoms in CP patients is essential for the entirely symptom-targeted management. Moreover, most of the interventional studies in this patient population rely on ratings of videos before and after treatment to measure the outcome. The only fair to moderate inter- and intra-observer agreement of symptom assessment found in our pilot study provides an extra warning against the usefulness of using solely video-based scoring of symptom severity. The highly variable effects of for instance DBS in dystonic CP might partially be explained by the use of videos as main outcome measure.

The effectiveness of management in CP and especially dystonia is challenging. Lumsden and colleagues already highlighted that solely looking at reduction in motor

Table 1 – Reported outcome, inter- and intra-observer agreement for the main symptom among the nine clinicians.

	Main symptom			Inter-observer agreement			Intra-observer agreement	
	Spastic n (%)	Dyskinetic n (%)	Ataxic n (%)	Agree (n)	Fleiss kappa (p-value)	Confidence interval	Agree (n)	Cohen's kappa (p-value)
All	86 (64)	47 (35)	2 (1)	6/15	0.36 (<0.0001)	0.28–0.44	54/72	0.51 (<0.0001)
PN	26 (58)	19 (42)	0 (0)	10/15	0.55 (<0.0001)	0.25–0.84	20/24	0.67 (<0.0001)
RP	31 (69)	13 (29)	1 (2)	8/15	0.33 (0.033)	0.02–0.57	18/24	0.50 (0.010)
MD	29 (65)	15 (33)	1 (2)	8/15	0.34 (0.014)	0.07–0.62	16/24	0.39 (0.024)

PN = pediatric neurologists; RP = rehabilitation physicians; MD = movement disorder specialists.

symptoms is not a reliable tool to measure treatment effect in this patient group. The focus should be more on improvement of functional domains of activity and social participation.[7] A small case series already showed that DBS in twelve children with dystonic CP was beneficial based on functional goal-achievement as primary outcome measure, without clear motor improvement.[11] These observations in combination with our findings, strongly point towards alternative outcome measures to evaluate therapeutic options in CP children.

In summary, this study shows that clinical phenotyping of children with CP using standardized videos has a large inter- and intra-observer variability. It is questionable if scoring the motor outcome on videos as primary outcome in treatment studies in CP are the most accurate tool to use. We therefore advocate to open the discussion about the phenotype and applicability to use the definitions of spasticity, dystonia and ataxia in CP patients. Future studies to measure the effectiveness of treatment such as DBS in dystonic CP upon functional domains are needed to assess the true impact of management options in this highly challenging patient population.

Ethical standards

The patient and her caregivers gave permission to the publication of this case report and videos. No permission was needed from the ethics committee for this case report.

Funding sources

The authors report no sources of funding.

Conflicts of interests

The authors declare that they have no conflict of interest.

REFERENCES

1. Bax M, Goldstein M, Rosenbaum P, et al. Proposed definition and classification of cerebral palsy, April 2005. *Dev Med Child Neurol* 2005;**47**(8):571–6. http://dx.doi.org/10.1017/S001216220500112X.
2. Sanger TD, Delgado MR, Gaebler-Spira D, Hallett M, Mink JW. Task force on childhood motor disorders. Classification and definition of disorders causing hypertonia in childhood. *Pediatrics* 2003;**111**(1):e89–97. http://dx.doi.org/10.1542/peds.111.1.e89.
3. Roubertie A, Rivier F, Humbertclaude V, et al. The varied etiologies of childhood-onset dystonia. *Rev Neurol Paris* 2002;**158**(4):413–24. http://www.ncbi.nlm.nih.gov/pubmed/11984483 [Accessed 31 August 2016].
4. Lin J-P. The contribution of spasticity to the movement disorder of cerebral palsy using pathway analysis: does spasticity matter? *Dev Med Child Neurol* 2011;**53**(1):7–9. http://www.ncbi.nlm.nih.gov/pubmed/21171216 [Accessed 1 September 2016].
5. Van Schaeybroeck P, Nuttin B, Lagae L, Schrijvers E, Borghgraef C, Feys P. Intrathecal baclofen for intractable cerebral spasticity: a prospective placebo-controlled, double-blind study. *Neurosurgery* 2000;**46**(3):603–9. discussion 609–612, http://www.ncbi.nlm.nih.gov/pubmed/10719857 [Accessed 1 September 2016].
6. Koy A, Hellmich M, Pauls KAM, et al. Effects of deep brain stimulation in dyskinetic cerebral palsy: a meta-analysis. *Mov Disord* 2013;**28**(5):647–54. http://dx.doi.org/10.1002/mds.25339.
7. Lumsden DE, Gimeno H, Tustin K, Kaminska M, Lin J-P. Interventional studies in childhood dystonia do not address the concerns of children and their carers. *Eur J Paediatr Neurol* 2015;**19**(3):327–36. http://dx.doi.org/10.1016/j.ejpn.2015.01.003.
8. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;**33**(1):159–74. http://www.ncbi.nlm.nih.gov/pubmed/843571 [Accessed 2 September 2016].
9. Sellier E, Horber V, Krägeloh-Mann I, De La Cruz J, Cans C, SCPE Collaboration. Interrater reliability study of cerebral palsy diagnosis, neurological subtype, and gross motor function. *Dev Med Child Neurol* 2012;**54**(9):815–21. http://dx.doi.org/10.1111/j.1469-8749.2012.04359.x.
10. Bax M, Tydeman C, Flodmark O. Clinical and MRI correlates of cerebral palsy: the European cerebral palsy study. *JAMA* 2006;**296**(13):1602–8. http://dx.doi.org/10.1001/jama.296.13.1602.
11. Gimeno H, Tustin K, Lumsden D, Ashkan K, Selway R, Lin JP. Evaluation of functional goal outcomes using the canadian occupational performance measure (COPM) following deep brain stimulation (DBS) in childhood dystonia. *Eur J Paediatr Neurol* 2014;**18**(3):308–16. http://dx.doi.org/10.1016/j.ejpn.2013.12.010.