Cognitive functioning in dyskinetic cerebral palsy: its relation to motor function, communication and epilepsy.

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Abstract

Background: Cerebral palsy (CP) is a disorder of motor function often accompanied by cognitive impairment. There is a paucity of research focused on cognition in dyskinetic CP and on the potential effect of related factors.

Aim: To describe the cognitive profile in dyskinetic CP and to assess its relationship with motor function and associated impairments.

Method: Fifty-two subjects with dyskinetic CP (28 males, mean age 24y 10mo, SD 13y) and 52 typically-developing controls (age- and gender-matched) completed a comprehensive neuropsychological assessment. Gross Motor Function Classification System (GMFCS), Communication Function Classification System (CFCS) and epilepsy were recorded. Cognitive performance was compared between control and CP groups, also according different levels of GMFCS. The relationship between cognition, CFCS and epilepsy was examined through partial correlation coefficients, controlling for GMFCS.

Results: Dyskinetic CP participants performed worse than controls on all cognitive functions except for verbal memory. Milder cases (GMFCS I) only showed impairment in attention, visuoperception and visual memory. Subjects with GMFCS II-III also showed impairment in language-related functions. Severe cases (GMFCS IV-V) showed impairment in intelligence and all specific cognitive functions but verbal memory. CFCS was associated with performance in receptive language functions. Epilepsy was related to performance in intelligence, visuospatial abilities, visual memory, grammar comprehension and learning.

Conclusion: Cognitive performance in dyskinetic CP varies with the different levels of motor impairment, with more cognitive functions impaired as motor severity increases. This study also demonstrates the relationship between communication and epilepsy and cognitive functioning, even controlling for the effect of motor severity.

Keywords: Cerebral palsy, cognition, motor function, communication, epilepsy.

1. Introduction

Cerebral palsy (CP) is one of the most common disabilities in childhood and it is permanent during all the life of the affected children, making heavy and constant demands on health, educational, and social services.[1,2] The overall prevalence of CP has remained constant in recent years despite the improvement in obstetric and neonatal practices and it is estimated at 2.11 per 1000 live births.[3] The term 'cerebral palsy' describes a group of permanent disorders of movement and/or posture and of motor function, caused by a non-progressive interference, lesion, or abnormality of the developing or immature brain. The motor disorders of CP are often accompanied by other impairments such as disturbances of sensation, perception, cognition, communication or epilepsy,[4] which become increasingly important due to their impact on everyday functioning and quality of life.[5]

As may be inferred from its definition, CP is a complex and heterogeneous motor disorder, making it absolutely necessary to establish some classification of cases. The Surveillance of Cerebral Palsy in Europe (SCPE) has classified the CP in three main groups according to their neurological signs: spastic, dyskinetic and ataxic. Dyskinetic CP is characterized by abnormal patterns of posture and/or movement, accompanied by involuntary, uncontrolled, recurring and occasionally stereotyped movements.[6] Compared to other types, dyskinetic CP is particularly disabling: almost 85% of the cases are unable to walk without aid and more than half suffer accompanying impairments, such as communication impairments, epilepsy and intellectual disability.[5–8]

Cognitive impairments are a very common problem throughout the entire CP spectrum. It is estimated that almost 50% of the CP population present intellectual disability (IQ <70) and 28% have a severe intellectual disability (IQ <50), being the latter more frequent in dyskinetic CP.[5] Most studies to date only report global estimates of intelligence rather than provide detailed information on specific cognitive functions. Characterizing specific cognitive profiles takes on great significance in the clinical and educational setting because it would allow designing more efficient rehabilitation and/or educational strategies, fitting better the real needs and capabilities of these people.[9–12] Furthermore, specific cognitive impairments have been shown to impact social abilities and participation in people with spastic CP, which in turn affect their learning and cognitive development.[13] However, most of these works have been carried out in cases with a slight degree of motor impairment, such as spastic hemiplegia or diplegia,[13,14] probably because cognitive assessment of people with severe motor and communicative impairments can be difficult. However, the functional and neuroimaging differences observed between types of CP prevent the generalisation of these results and highlight the need to conduct studies focusing specifically on dyskinetic cases.[15,16] In contrast to spastic CP, which is more prevalent in preterm-born children, dyskinetic CP is reported to occur especially in term-born children and it has been more frequently associated with peri- or neonatal adverse events, leading to a different pattern of brain injury.[1] The main neuroimaging finding in dyskinetic CP is basal ganglia and thalamus lesions combined with cortical injury, while spastic CP is predominantly associated to periventricular white matter lesions. However, several studies have recently shown evidence of white matter damage in people with dyskinetic CP.[17–19] As particular consequences and needs of individuals with dyskinetic CP are less known, the current interventions and follow-up programs are mainly based on the most prevalent and known type of CP, spastic CP.

The lower frequency and greater physical and communicative impairments of people with dyskinetic CP could explain why cognitive studies of this form are scarce. Most studies compare their cognitive performance with people with spastic CP, noting that dyskinetic subjects have lower IQ[20] and poorer verbal performance, especially in expressive skills.[21] Few studies have focused on receptive communication, probably because the assessment of language comprehension is difficult in people with limited behavioral and speech repertoire.[22] Subjects with dyskinetic CP were found to perform better than spastic children in language comprehension despite a comparable level of gross motor (GMFCS IV and V) and expressive communication (non-speaking).[23] Nevertheless, when all degrees of severity are taken into account the results are inconclusive.[21,24–26] Comparing their performance to population-based norms, participants with bilateral dyskinetic CP did not manifest impairment in receptive grammatical abilities but all exhibited poor vocabulary.[26] However, this study only included six subjects with dyskinetic CP.

Regarding visual-perceptual abilities, early research indicated that visual-perceptual and visual-motor impairments were related to the type of CP, being the spastic more affected than the dyskinetic.[27] However, there are also evidences reporting that dyskinetic CP has more perceptual and visual-motor impairments than spastic CP or that did not find differences among groups.[27,28] These conflicting results have led to a recent systematic review to conclude that CP subtype has not demonstrated a consistent impact across studies,[29] although the few studies that included subjects with dyskinetic CP had small sample sizes. Further research is needed in order to elucidate the visual-perceptual performance in dyskinetic CP.

Attention, memory and executive functions have been the least studies cognitive functions in dyskinetic CP. The few data available would point to a better immediate and working memory performance in people with dyskinetic CP than spastic CP, although they could present difficulties in declarative memory and some executive functions.[25,26] However, these findings should be considered with caution since they are based on a small sample size.

The lack of studies comparing dyskinetic CP subjects with a control group makes it difficult to draw any firm conclusions concerning their cognitive functioning, so that the current interventions are not yet adapted to the specific characteristics of people with dyskinetic CP.[12,30,31] Moreover, certain functional variables such as motor function, communication and the presence of epilepsy have been found to influence general cognitive performance in spastic CP,[32,33] but their effect on specific cognitive performance in dyskinetic CP is still unknown. Thus, the aims of the present study are 1) to describe the cognitive profile of people with dyskinetic CP compared to typically-developing controls, and taking into account motor severity and 2) to assess the relationship between cognitive performance and associated impairments such as communicative impairments or the presence of postnatal epilepsy.

2. Materials and Methods

2.1. Design and procedure

A case-control study was carried out. Participants were recruited from the Hospital Vall d'Hebron (Pediatric Neurology Department and Rehabilitation and Physical Medicine Department), the Hospital Sant Joan de Déu (Neurology Department), the Cerebral Palsy Association ASPACE (Health services and rehabilitation), and from a previous study.[26] Participants were recruited and data were collected between 2012 and 2015. The study was approved by the University of Barcelona's Institutional Ethics Committee, Institutional Review Board (IRB 00003099, assurance number: FWA00004225; http://www.ub.edu/recerca/comissiobioetica.htm). The research was conducted in accordance with the Helsinki Declaration. Signed consent was obtained from all participants or their caregivers.

2.2. Participants

The inclusion criteria were: 1) clinical diagnosis of CP with predominant dyskinetic features, 2) age over six years old, 3) presence of an intelligible yes/no response system, and 4) being able to understand simple instructions as assessed by the Screening Test of Spanish Grammar (receptive part).[34] The presence of hearing abnormalities or severe visual difficulties that precluded neuropsychological assessment was considered as an exclusion criterion, along with a current history of substance use disorder.

Out of a total of 101 potentially eligible participants, 26 declined to participate, nine could not be localized and two who were being treated for substance use disorder were excluded. The remaining 64 cases agreed to participate, but seven did not meet the criteria of an intelligible yes/no response system and of understanding simple instructions, and five abandoned. The final sample consisted of 52 cases with dyskinetic CP: 18 children (7 – 17y), 21 young adults (18 – 30y), and 13 adults (>30y) [table 1].

Fifty-two typically-developing people matched by age and gender were recruited as a comparison group (28 males, mean age 24y 8mo, SD 12y 9m, age range 7 – 60). Controls were ineligible if they were preterm (<37 weeks of gestational age), had history of neurological or psychiatric disorder, or were substance-abusing.

2.3. Assessments

2.3.1. Motor status

Motor function was assessed following the recommendations of the Surveillance of Cerebral Palsy in Europe: the Gross Motor Function Classification System (GMFCS)[35] for lower limb function and the Bimanual Fine Motor Function (BFMF)[36] and the Manual Ability Classification System (MACS)[37] for the upper limbs. These three scales were developed to characterize mobility and manual function in CP. They use a 5-level classification system (from I to V) and higher scores indicate lower levels of motor functioning.

2.3.2. Communication

Daily communication performance was assessed by means of the Communication Function Classification System (CFCS)[38]. The CFCS also ranges from I to V with higher scores indicating lower levels of communication in terms of effectiveness and velocity of the communication. The CFCS level was determined based on the information obtained through an interview with relatives along with the interaction with the participant itself.

2.3.3. Epilepsy

The International League Against Epilepsy criteria were used to determine epilepsy status: active epilepsy, resolved epilepsy or non-epilepsy.[39] Following these criteria, active epilepsy was defined as 1) a history of at least two unprovoked seizures occurring >24 h apart, excluding neonatal seizures; or 2) a history of one unprovoked seizure, excluding neonatal seizures, with drug treatment administered. Resolved epilepsy was considered in cases that have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years. For statistical analyses, subjects with active and resolved epilepsy were merged into the same group and compared to those with no history of postnatal epilepsy.

2.3.4. Cognitive assessment

Participants completed a comprehensive neuropsychological battery, including the following cognitive functions and tests: intelligence (Raven's Colored Progressive Matrices[40]), visual and verbal attention (Spatial and Digit Span subtests on the Wechsler scales[41–43]), visuospatial and visuoperceptual abilities (Benton's Judgment of Line Orientation Test and Facial Recognition Test[44]), receptive vocabulary (Peabody Picture Vocabulary Test-3rd [45]), basic grammar comprehension (Screening Test of Spanish Grammar, receptive part[34]), verbal learning (Rey Auditory Verbal Learning Test[46]), visual and verbal memory (Pattern and Verbal Recognition Memory subtests of the Cambridge Neuropsychological Test Automated Battery[47]) and cognitive flexibility (Wisconsin Card Sorting Test-64[48]). A brief description of each test as well as the specific scores used can be found in Supporting Information [Appendix A].

These tests are extensively used in neuropsychological assessment and most of them allow a nonverbal response. In addition, priority was also given to those tests that minimized the motor skills involved and that do not take into account the execution time, since this could penalise subjects with CP. It should be noted that the original tests were used and that the items were not altered. Only the administration of the Verbal Recognition Memory subtest was slightly modified (see Supporting Information [Appendix A]). Adaptations were only introduced in order to encourage subjects to answer in an autonomous way. Participants were allowed to use the communication devices they normally used, and the response technique that best fitted their abilities was chosen. In this manner, subjects answered the tests orally and/or pointing (with finger or hand, an adapted pointer on the head or fixing the gaze if the original distribution of multiple choices allowed it). To access the computer tests, a mouse/joystick (controlled by hand or with the chin) and two switches (pressed by hand, cheek or head) were used. In those cases in which autonomous response was not possible, the examiner indicated the various response alternatives while asking the participant if it was his/her choice.[9] These subjects answered "yes" or "no" by means of vocalizations, movement of head, facial miming or gestures with other parts of the body, as they usually did. For more details on the specific adaptations used for each test see Supporting Information [Appendix A].

Twelve subjects had one or more missing values because they had some difficulty that prevented them from completing the test, such as: 1) non-verbal communication, which precluded the verbal learning test, 2) inability to point by any method due to a generalized motor severity, usually accompanied by insufficient control of the gaze, 3) a very slow communication system requiring much effort from the subject and increasing their fatigue level, especially on long tasks, and 4) comprehension difficulties that prevented understanding some of the most complex tasks. Detailed information about sample sizes for each test is included in Supporting Information [Appendix A].

2.4. Statistical analysis

Statistical analyses were performed using SPSS version 22 (IBM SPSS Statistics, IBM Corp. NY, USA) and MATLAB (MATLAB 2013a, The MathWorks, Inc., Batick, MA, USA). The normality of distribution was tested using the Shapiro–Wilk test. The level of significance was set at *p*-value less than .05. Missing data were managed with pairwise analyses. A *t*-test or Mann-Whitney analysis was applied to compare the cognitive performance between the CP group and control group, both overall and separating them by GMFCS level. Subjects were grouped as GMFCS I (able to walk without aid), GMFCS II–III (able to walk with aid), and GMFCS IV–V (unable to walk). We used Bonferroni corrected *p* values to reduce the chance of type I error. In this work, cognitive impairment has been defined in relation to the performance of typically-developing controls, so it will be considered alteration when there is a significant difference in raw scores between CP and typically-developing subjects. The effect size was calculated with Pearson's correlation coefficient *r* statistic, interpreting 0.10 as small, 0.30 as medium and 0.50 as large.[49]

Partial Spearman's correlation coefficients were carried out to check the relationship between associated impairments (CFCS level and presence of epilepsy) and cognitive performance, controlling for the effect of age and level of motor impairment (GMFCS). All analyses were performed with and without the outliers. As the results did not change as a consequence of removing outliers except in one analysis, these cases were retained. In the analysis where the result did change, the outlier was removed.

3. Results

Performance of all subjects with dyskinetic CP was significantly poorer than in controls in all cognitive functions except for short and long term verbal memory, which was no longer significant after Bonferroni correction [table 2]. As for different levels of motor function (GMFCS), subjects with mild to moderate motor impairment (GMFCS levels I and II-III) performed significantly poorer than typically-developing subjects on attention, visuospatial and visuoperceptual abilities, and visual memory; subjects with moderate motor impairment (GMFCS levels II-III) also had significantly lower scores on language-related tests (receptive vocabulary, basic grammar comprehension and verbal learning); finally, subjects with severe motor impairment (GMFCS levels IV-V) performed significantly worse than controls on all cognitive functions except for verbal memory [table 3]. However, some subjects in the group with more severe motor impairment presented average performance (see Supporting Information, Appendix B).

With regard to associated impairments, after controlling for age and GMFCS level, poorer daily communication and the presence of epilepsy were associated with lower cognitive performance in some cognitive functions. Specifically, daily communication (CFCS) was negatively correlated with performance in verbal attention (r_s=-0.38, p=0.01), receptive vocabulary (r_s=-0.4, p=0.004), basic grammar comprehension (r_s=-0.41, p=0.003) and visual short term memory (r_s=-0.29, p=0.04). The presence of epilepsy was associated with poorer performance in intelligence (r_s=-0.37, p=0.009), visuospatial abilities (r_s=-0.45, p=0.001), basic grammar comprehension (r_s=-0.36, p=0.01), verbal learning (r_s=-0.36, p=0.02) and visual short term memory (r_s=-0.29, p=0.04).

4. Discussion

This study describes the cognitive profile of 52 subjects with dyskinetic CP in relation to a group with a typical development, as well as analyses the relationship between cognitive performance and the level of motor impairment, communication performance and the presence of postnatal epilepsy.

The results show that the cognitive performance of people with dyskinetic CP is lower than that of typically-developing subjects in all the functions assessed, except for verbal memory (short and long term). This finding partially agrees with the results of Pueyo et al. (2009), who found that none of the 6 subjects with dyskinetic CP showed impaired verbal short term memory.[26] However, they noted difficulties in verbal long term memory in four of the five cases with dyskinetic CP, which is not consistent with the results of our study.[26] This discrepancy may have stemmed from the use of a more complex word-list recognition task used in Pueyo et al. (2009), which contained 50 stimuli compared with only 12 in our study.[26] This long term memory impairment found in Pueyo et al. (2009) together with the learning difficulties found in our work, would fit with recent neuroimaging studies showing hippocampal involvement in dyskinetic CP. Park et al. (2014) found a reduction in the volume of the hippocampus and the parahippocampal gyrus[50] and Ballester-Plané et al. (2017) demonstrated altered hippocampal connectivity.[18] This long-term memory impairment that seems to emerge when the number of stimuli increases could also be associated with executive impairment, also found in our CP group with greater motor impairment. White & Christ (2005), for instance, concluded that the learning and memory difficulties found in bilateral spastic CP (difficulties in strategic processing and recognition) were more related to prefrontally-mediated executive aspects than to associative aspects mediated by medial-temporal brain regions.[51] Further studies are needed to elucidate the controversy over memory performance in dyskinetic CP, due to the importance that memory can have in school learning and academic performance..

The first noteworthy finding when we separate CP and typically-developing subjects according to GMFCS level is that as motor severity increases, more cognitive functions are impaired compared to healthy controls. These results are in line with previous reports of a strong negative correlation between GMFCS and intellectual level,[15,20,32] although this association between motor impairment and specific cognitive functions had not been reported so far. The association between GMFCS and cognitive functioning could be explained by the severity of the underlying brain injury, since more diffuse brain injury has been associated not only with more severe motor problems[18,52,53] but also with greater cognitive impairments.[18,19,54]

Furthermore, it is important to highlight the functions that are impaired compared to typically-developing subjects even in milder cases. Subjects at any GMFCS level performed significantly worse than healthy controls in attention, visuoperception, and visual memory. These attentional difficulties may be due to the involvement of basal ganglia and thalamic functional systems,[13] found in 67% and 73% of the subjects of this study, respectively. Recent research has attributed more complex roles for the basal ganglia in processing higher cognitive functions, such as executive and attentional functions, across the neural circuits linking these structures with cortical areas.[55,56] Moreover, several cortico-subcortical connections have been found to be altered in people with dyskinetic CP and this have also been associated with cognitive impairments in this population.[18,19] As for visuoperceptual impairments, our results show evidence of their occurrence in a large sample of people with dyskinetic CP, thus providing further support for the findings of Ego et al. (2015), who come to the conclusion that visuoperceptual impairments are a core disorder in the entire CP syndrome regardless of the subtype.[29] The impairment found on visual memory task may also be related to these visuoperceptual deficits, which have been associated with a relative fragility in visual memory processes.[57] We consider these findings to be of utmost importance, since they indicate that even mild motor cases may have specific cognitive difficulties, specifically in attention and functions involving visuoperception. Attention is a basic function that has in itself a large impact on several developmental and cognitive domains and visuoperceptual difficulties hinder normal visuomotor development, influencing visually guided motion and having an impact in mobility, self-care and social function.[58–61] Visual perceptual impairments have been also found to negatively influence the formation of visual data-bank, slowing down the development of categorization and the outgrowth of visual memory and other visually-based functions.[62,63] These data should lead us to consider the fact of including cognitive stimulation of these functions in the current early intervention programs for these patients, with the aim of trying to minimize as much as possible these later cognitive difficulties. Evidence already exists on the effectiveness of early intervention programs to improve visuoperceptual outcomes.[64]

Another point that should be stressed is that subjects with a GMFCS level of I, II and III performed as good as healthy controls on certain functions, such as intelligence or cognitive flexibility. Using the Raven's Colored Progressive Matrices to analyze non-verbal intelligence in children with different types of CP, Smits et al. (2011) also showed that the performance of subjects with GMFCS level I and II was close to that of typically-developing children.[65] In relation to executive functions, our results do not confirm the findings of Pueyo et al. (2009) who found executive deficits in the five participants with dyskinetic CP who were evaluated, regardless of the level of motor impairment.[26] Our results partially agree with those of Nadeau et al. (2008), who found worse performance in cognitive flexibility at higher levels of motor impairment in children with spastic CP.[66] The fact that executive functions follow a protracted development pattern from infancy to late adolescence and that encompass several different components, makes it necessary to carry out a comprehensive study analyzing the effect of age as well as all the executive components in people with dyskinetic CP. Despite the similarities, the main difference between CP subjects with GMFCS level I and levels II-III appears in language-related tests. While CP subjects with GMFCS level I show no differences with regard to healthy controls, subjects with level II-III performed significantly worse than typically-developing controls in receptive vocabulary, basic grammar comprehension and verbal learning. This could be due to the fact that at these GMFCS levels subjects have some communication difficulties,[7,67–69] as shown in our sample. This finding agrees with previous research in which the severity of CP was positively associated with expression and comprehension problems.[33]

The second goal of this study was to analyze the relationship between cognitive performance and associated impairments such as communication difficulties and the presence of epilepsy, controlling for the effect of age and motor impairment. This will allow us to broaden our knowledge of the cognitive difficulties of these subjects, not only knowing their manifestations in terms of motor impairment but also in relation to some commonly associated deficits. Regarding communication, results showed that poorer daily communication was associated with lower performance mainly in receptive language-related functions (verbal attention, receptive vocabulary and basic grammar comprehension). This finding may be related to the fact that motor difficulties that inhibit speech ability in dyskinetic CP affect the frequency and the quality of communicative acts,[15,33,70] which in turn can hinder the understanding of some aspects of spoken language such as grammar comprehension, as suggested by Pueyo et al. (2013).[71] This work showed that expression abilities contributed to explain grammar comprehension skills in a sample of people with different types of CP.[71] In the same direction, Mei et al. (2015) concluded that co-occurring expressive and receptive language impairment was common in a population-based study of children with CP.[72] These findings highlight the importance of effective communication for the proper development of several language-related functions in dyskinetic CP. This stresses the importance of the clinical intervention to improve communicative skills in this population, since effective modes of communication are closely related to both social development and academic progress.[24]

As for the presence of epilepsy, our results show that it is associated with poorer performance on intelligence, visual functions (visuospatial abilities and visual memory) and verbal functions (grammar comprehension and verbal learning). Several studies have reported the association between epilepsy and lowered cognitive functioning in children with spastic CP.[20,32] Sigurdadottir et al. (2008) found that epilepsy had an independent effect on intelligence in children with CP and that epilepsy along with GMFCS explained 22% of its variance.[20] With regard to visuoperceptual impairments, the results are contradictory. Stiers et al. (2002) found no relationship between epilepsy and visuoperceptual performance,[73] whereas Gonzalez-Monge et al. (2009) found a clear negative effect of epilepsy on non-verbal intelligence in a longitudinal study with unilateral spastic CP.[74] However, clearer results have been found in relation to visual memory, since seizures are known to adversely affect memory performance in CP.[75,76] In relation to verbal functions, epilepsy have been found to be related to restrictions in communication.[24,77–79] As far as we know, only the study of Geytenbeek et al. (2015) analyzed the relationship between epilepsy and language comprehension in children with CP, and did not find an association between both variables.[23] The fact that the study only included severe cases and that did not separate by type of CP when the relationship between epilepsy and language comprehension was analyzed could explain the difference between studies. Finally, our results highlight that the presence of epilepsy is associated with poorer verbal learning performance, as studies in other populations and other types of CP have found.[75,80] The recent findings suggesting epilepsy as a disorder involving widespread brain networks[81] may fit with the fact that dyskinetic CP has recently been associated with a diffuse pattern of brain injury, including white matter connections of the different lobes,[18] which have already been associated with impairments in specific cognitive functions.[54,82,83]

It should be noted that the relationship between cognitive performance and associated impairments was found even controlling for the effect of motor severity. This finding underscores the importance of associated impairments by themselves and their impact in cognitive performance regardless of motor involvement, providing further evidence that symptoms of CP go beyond motor impairments. This could, otherwise, explain why even in the most severe group some subjects may present an average performance compared to typically-developing controls (see Supporting Information, Appendix B). Finally, another noteworthy aspect is the presence of a lower performance in visuoperception, language functions and learning without evidence of a decrease in overall cognitive performance compared to the control group in mild to moderate cases (GMFCS I, II and III). This finding highlights the importance of carrying out a comprehensive neuropsychological assessment in this population in order to identify specific cognitive difficulties that go beyond general cognitive performance. Comprehensive intervention programs are required to include cognitive rehabilitation strategies as a crucial aspect for the future development and the quality of life of people with CP. The present findings should also lead us to consider the need to customize clinical interventions according to the specific difficulties, needs and capacities of each person with CP.

4.1. Strengths and limitations

This is the first study to carry out a comprehensive neuropsychological assessment in a wide sample of people with this particularly disabling form of CP. Identifying the particular cognitive features of individuals with dyskinetic CP is crucial for a better understanding of this little known subtype, and may contribute to the design of more appropriate interventions and follow-up programs. Recent studies have begun to apply deep brain stimulation to patients with dyskinetic CP,[84] a fact that has raised questions about the non-motor effects of this treatment, in particular in cognitive functions.[85] In order to delve into these issues, a clear description of the cognitive profile of these patients is absolutely necessary, especially considering the level of performance and the influence of the associated deficits. However, this study has a number of limitations. First, the lack of a well-established measure of the dyskinesia component in CP when this research started, hence our study was only based on general clinical criteria. Secondly, the lack of population-based norms for some of the included tests may have clinical relevance, since the alteration or preservation of cognitive functions in dyskinetic CP subjects was established in comparison to the performance of a typically-developing group matched by age and gender. Continuing with this, CP and control groups were matched by age and gender, but not by other variables that may influence cognitive performance such as parental educational level or socioeconomic status. Regarding the grouping of CP subjects, it would have been interesting to analyze the effect of epilepsy by separating those subjects with active and resolved epilepsy. The wide age range of the sample is another drawback, even though the groups were age-matched and age was added as a covariate in the correlation analysis. The fact that this is not a population-based study and that the most severe cases cannot be included in a study of this nature also limits the generalizability of the results to the whole spectrum of dyskinetic CP. Finally, it is noteworthy that the visuoperceptual difficulties demonstrated in these subjects may be interfering with their performance in other tests including visual elements. This is a clear limitation in the field, since there is a lack of appropriate standardized cognitive measures for people with severe motor, communicative and visual impairments.[86] Nevertheless, we must emphasize that we are facing a study with a relatively wide sample if we take into account the low frequency of this type of CP, the characteristics of these patients and the previous studies performed. We consider that future studies should evaluate executive functioning in a more extensive way by taking all its components into account.

5. Conclusion

Performance in people with dyskinetic CP is in general lower than in their peers in several cognitive functions, with the exception of verbal memory. Neuropsychological performance varies with the different levels of motor impairment. Cases with mild motor involvement (GMFCS I) only show a lower performance than healthy controls in attention, visuoperception and visual memory. Subjects with moderate motor impairment (GMFCS II and III) also show difficulties in language-related functions and learning, whereas severe cases (GMFCS IV and V) show a lower performance in intelligence as well as in all specific cognitive functions except for verbal memory. Greater cognitive impairment is observed as severity increases, although even in the most severe group some subjects present average performance compared to healthy controls. Finally, the relationship between associated impairments and cognitive performance in specific cognitive functions has been demonstrated, even controlling for the effect of motor severity. Poorer daily communication was associated with lower performance mainly in receptive language functions, evidencing the relationship between expressive and receptive language. The presence of epilepsy was associated with poorer performance in intelligence, visual functions (visuospatial abilities and visual memory) and verbal functions (grammar comprehension and verbal learning).

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Table 1

Characteristics of dyskinetic CP participants, divided by GMFCS levels and as total sample.

Demographic and clinical data	**CP GMFCS I (n=15)**	**CP GMFCS II/III (n=14)**	**CP GMFCS IV/V (n=23)**	**Total CP sample (n=52)**
Mean age (SD)	21y 4m (8y 6m)	22y 6m (12y 3m)	28y 6m (15y 2m)	24y 10m (13y)
Age range	7 - 41	9 - 51	11 - 62	7 - 62
Children (7 – 17y)	4	7	7	18
Young adults (18 – 30y)	9	4	8	21
Adults (>30y)	2	3	8	13
Gender, n (female/male)	9/6	4/10	11/12	24/28
Motor involvement, n				
Unilateral	6	2	0	8
Bilateral	9	12	23	44
GMFCS, n				
I	15	-	-	15
II	-	8	-	8
III	-	6	-	6
IV	-	-	11	11
V	-	-	12	12
BFMF, n				
I	6	1	0	7
II	7	4	1	12
III	1	7	8	16
IV	1	2	9	12
V	0	0	5	5
MACS, n				
I	5	0	0	5
II	7	2	1	10
III	3	10	4	17
IV	0	2	8	10
V	0	0	10	10
CFCS, n				
I	11	3	3	17
II	4	10	9	23
III	0	1	5	6
IV	0	0	6	6
V	0	0	0	0
Gestational age, n				
<32 weeks	0	1	3	4
32-36weeks	2	1	3	6
≥37 weeks	13	12	17	42
Weight at birth, n				
<1500 g	0	1	2	3
1500 – 2499 g	3	1	4	8
2500 – 3499 g	5	7	9	21
≥3500 g	6	4	5	15
Unknown	1	1	3	5
Epilepsy status, n				
No epilepsy	12	9	9	30
Active	3	4	9	16
Resolved	0	1	5	6

Neuroimaging findings				
Normal	1	0	1	2
Maldevelopment	1	3	2	6
White matter lesion	2	4	15	21
Cortical grey matter	1	0	1	2
Basal ganglia	11	9	15	35
Thalamus	8	10	20	38
Aetiology				
HIE	4	7	11	22
Intra-cranial haemorrhage/infarction /hydrocephalus	4	2	3	9
Infection	0	2	0	2
Kernicterus	1	1	0	2
Unclassifiable	6	2	9	17

BFMF: Bimanual Fine Motor Function; CFCS: Communication Function Classification System; CP: cerebral palsy; GMFCS: Gross Motor Function Classification System; HIE: Hypoxic-ischemic encephalopathy; MACS: Manual Ability Classification System; SD: standard deviation.

Table 2

Comparison of raw test scores between dyskinetic CP and typically-developing subjects.

Neuropsychological functions	CP (n= 52)	TD (n=52)	T/U (p)	r
Intelligence	27.5 (11)	35 (2)	**445 (<.001)** †	-0.58
Visual attention	14 (8)	19 (4)	**307.5 (<.001)** †	-0.63
Verbal attention	12.57 (4.45)	17.54 (3.46)	**-5.91 (<.001)**	0.52
Visuospatial abilities	15 (18)	29 (3)	**361 (<.001)** †	-0.62
Visuoperception	43 (6)	49 (7)	**433 (<.001)** †	-0.59
Receptive vocabulary	129 (57)	167 (25)	**525.5 (<.001)** †	-0.53
Basic grammar comprehension	44.75 (4.8)	46 (0)	**680.5 (<.001)** †	-0.52
Verbal learning*	48.5 (22)	56.5 (9)	**303.5 (<.001)** †	-0.53
Visual short term memory	19 (5)	23 (3)	**525.5 (<.001)** †	-0.52
Visual long term memory	8 (3)	11 (2)	**564.5 (<.001)** †	-0.49
Verbal short term memory	23 (4)	23 (2)	954.5 (.016) †	-0.24
Verbal long term memory	22 (4)	23 (3)	1003 (.042) †	-0.2
Cognitive flexibility	2 (3)	3.5 (2)	**814.5 (.002)** †	-0.31

*Verbal learning task was only administered to subjects who were able to communicate through verbal communication (n = 40); †Non-parametric test was applied (Mann-Whitney test) and median (IQR) is indicated. Otherwise, parametric test was applied (*t*-test) and mean (SD) values are presented; In bold: Significance level set to .004 based on Bonferroni correction; CP: cerebral palsy; T: *t*-test; TD: typically-developing; U: Mann-Whitney test.

Table 3

Comparison of raw test scores between dyskinetic CP and typically-developing subjects, divided by level of GMFCS.

Neuropsychological functions	CP GMFCS I (n= 15)	TD (n=15)	T/U (p)	r	CP GMFCS II/III (n= 14)	TD (n=14)	T/U (p)	r	CP GMFCS IV/V (n= 23)	TD (n=23)	T/U (p)	r
Intelligence	33 (7)	34 (3)	76.5 (.137)†	-0.28	28.5 (10)	35 (3)	42.5 (.009)†	-0.49	25 (12)	36 (2)	**29.5 (<.001)**†	-0.77
Visual attention	15.20 (3.88)	19.93 (3.34)	**-3.51 (.002)**	0.56	13.57 (4.57)	18.21 (2.86)	**-3.22 (.003)**	0.53	9.47 (5.38)	19.37 (2.03)	**-7.5 (<.001)**	0.78
Verbal attention	14.27 (3.35)	18.13 (3.4)	**-3.14 (.004)**	0.51	13.43 (4.75)	18.29 (3.65)	-3.04 (.005)	0.51	10.5 (4.4)	16.33 (3.55)	**-4.38 (<.001)**	0.6
Visuospatial abilities	24 (16)	28 (2)	**38.5 (.001)**†	-0.56	15 (15)	28.5 (4)	**32 (.002)**†	-0.58	8 (20)	29 (4)	**46.5 (<.001)**†	-0.7
Visuoperception	45 (6)	50 (7)	**44.5 (.004)**†	-0.52	41.93 (5.54)	48.5 (5.47)	**-3.16 (.004)**	0.53	41 (5.82)	48.57 (3.25)	**-5.44 (<.001)**	-0.68
Receptive vocabulary	145 (42)	167 (36)	58 (.023)†	-0.41	123.43 (38.76)	159.79 (18.43)	**-3.17 (.004)**	0.53	114 (53)	165 (25)	**74.5 (<.001)**†	-0.62
Basic grammar comprehension	46 (4)	46 (0)	94.5 (.461)†	-0.2	44 (3.3)	46 (0)	**34 (.002)**†	-0.63	44 (8)	46 (0)	**99.5 (<.001)**†	-0.63
Verbal learning	49.33 (13.72)	58.73 (5.54)	-2.46 (.024)	0.42	38.57 (14.45)	57 (6.19)	**-4.39 (<.001)**	0.65	49 (22)*	56 (7)	**15 (.002)**†	-0.64
Visual short term memory	20 (6)	23 (4)	76.5 (.137)†	-0.28	19.5 (5)	23 (3)	**35 (.003)**†	-0.55	18 (4)	23 (2)	**62 (<.001)**†	-0.64
Visual long term memory	8 (2)	11 (2)	**42.5 (.003)**†	-0.54	8.14 (2.18)	9.79 (1.53)	-2.31 (.029)	0.41	9 (4)	11 (3)	**99 (.001)**†	-0.51
Verbal short term memory	23 (2)	23 (3)	111.5 (.967)†	-0.01	21.5 (4)	23 (3)	53 (.039)†	-0.4	23 (5)	24 (2)	165 (.048)†	-0.3
Verbal long term memory	22 (3)	23 (4)	112.5 (1)†	0	21 (4)	23 (3)	65 (.137)†	-0.29	22.5 (6)	23.5 (2)	165 (.062)†	-0.28
Cognitive flexibility	2.87 (1.46)	3.2 (1.47)	-.62 (.538)	0.12	2.36 (1.6)	3 (1.41)	-1.13 (.27)	0.22	2 (2)	4 (3)	**102.5 (.003)**†	-0.47

*Verbal learning task was only administered to subjects who were able to communicate through verbal communication (n = 11); [†]Non-parametric test was applied (Mann-Whitney test) and median (IQR) is indicated. Otherwise, parametric test was applied (*t*-test) and mean (SD) values are presented; In bold: Significance level set to .004 based on Bonferroni correction; CP: cerebral palsy; GMFCS: Gross Motor Function Classification System; T: *t*-test; TD: typically-developing; U: Mann-Whitney test.