Doi: 10.47572/muskutd.1440247

The Evaluation of Basal Ganglia in Pediatric Patients with Cerebral Palsy Using Magnetic Resonance Histogram Analysis

Serebral Palsili Pediatrik Hastalarda Bazal Ganglionların Manyetik Rezonans Histogram Analizi Kullanılarak Değerlendirilmesi

Ferit DOGAN[1], Mehmet DEMİR[1], Huseyin GUMUS[2], Celil YILMAZ[3]

[1]Harran University, Faculty of Medicine, Department of Radiology, Sanliurfa, Turkey
[2]Harran University, Faculty of Medicine, Department of Pediatrics, Sanliurfa, Turkey
[3]Sanliurfa Training and Research Hospital, Department of Pediatric Neurology, Sanliurfa, Turkey

Öz

Konvansiyonel manyetik rezonans görüntüleme (MRG) görüntülerinde bazal ganglionlarda patolojik sinyal değişiklikleri olmayan serebral palsili (SP) hastalarda MRG histogramını kullanarak bazal ganglionlardaki değişiklikleri tespit etmeyi amaçladık. Serebral palsili 40 çocuk ve beyin MRG incelemesinde anlamlı intrakraniyal bulgusu olmayan 60 çocuğun görüntüleri retrospektif olarak değerlendirildi. Ortalama, varyans, çarpıklık, basıklık, 1. yüzdelik (P), 10. P, 50. P, 90. P ve 99. P histogram parametreleri her hasta ve kontrol grubu için talamus, lentiform ve kaudat nukleuslardan tanımlanan alanlarda hesaplandı ve her vaka için ayrı ayrı değerlendirildi. Talamustan elde edilen histogram parametrelerinin ortalama, basıklık ve 50. P değerleri açısından gruplar arasında anlamlı fark bulundu (sırasıyla p=0.001, p=0.002, p=0.025). Lentiform çekirdeklerden elde edilen histogram parametrelerinin ortalama, çarpıklık, basıklık ve 1. P değerleri arasında anlamlı bir fark bulunmuştur (sırasıyla p=0.021, p=0.005, p=0.015, p=0.035). Nukleus kaudatustan elde edilen histogram parametrelerinin ortalama, basıklık, 90. P ve 99. P değerleri arasında anlamlı farklılık tespit edildi (sırasıyla p=0.002, p=0.03, p=0.004, p=0.042). Doku analizi, serebral palsili hastalarda bazal ganglionlar ve talamustaki farklılıkları gösterebilecek objektif özellikler üretebilir. Doku analizi, konvansiyonel MRG görüntülerinde patolojik sinyal değişikliği olmayan SP'li hastalarda bazal ganglionlardaki değişiklikleri tanımlayabilir.

Anahtar Kelimeler: Bazal Ganglionlar, Doku Analizi, Serebral Palsi, Talamus

Abstract

The aim of this study is to detect changes in the basal ganglia using magnetic resonance imaging (MRI) histogram in patients with cerebral palsy (CP) who do not have pathological signal changes in the basal ganglia on conventional MRI images. A retrospective evaluation was made of the images of 40 children with CP and 60 children with no significant intracranial findings on brain MRI examination. The histogram parameters of mean, variance, skewness, kurtosis, 1st percentile (P), 10th P, 50th P, 90th P and 99th P were calculated for each patient and control group on the areas identified in the head of the thalamus, lentiform nucleus and nucleus caudatus and these were evaluated separately for each case. A significant difference was found between the groups in terms of the mean, kurtosis and 50th P values of histogram parameters obtained from the thalamus (p=0.001, p=0.002, p=0.025, respectively). A significant difference was found between the mean, skewness, kurtosis and 1st P values of histogram parameters obtained from the lentiform nuclei (p=0.021, p=0.005, p=0.015, p=0.035, respectively). A significant difference was found between the mean, kurtosis, 90th P and 99th P values of the histogram parameters obtained from the head section of the nucleus caudatus (p=0.002, p=0.03, p=0.004, p=0.042, respectively). Texture analysis can produce objective features that may indicate differences in the basal ganglia and thalamus in patients with CP. Texture analysis can identify changes in the basal ganglia in patients with CP who do not have pathological signal changes on conventional MRI images.

Keywords: Basal ganglia, Texture analysis, Cerebral palsy, Thalamus

Introduction

Cerebral palsy (CP) is a condition that occurs with permanent disorders in motor functions, mostly in infants with very low birth weight (<1500 g), resulting from damage to the immature brain (1). Although the prevalence of CP varies with different birth weights and gestational ages, it is approximately 2 to 3 per 1,000 live births (2). CP is considered a clinical condition rather than an etiological diagnosis (3), and may present with many problems such as hearing, vision, learning disorders and epilepsy (4,5).

Different cerebral abnormalities have been observed on magnetic resonance imaging (MRI) in children with CP. Deep gray nuclei and the cortex may be affected. Gray matter damage occurs in approximately 14% to 22% of children with CP (6). Gray matter damage is associated with perinatal hypoxia-ischemia/hypotension, and in some etiological cases, it may also occur in infection, kernicterus, bleeding and hypoglycemia (7).

The importance of MRI as neuroimaging in the diagnosis of CP is increasing (8). The MRI classification system for children with CP has been used qualitatively to indicate maldevelopments, predominant white matter injuries, predominant gray matter injuries, miscellaneous and normal findings (9).

The aim of this study was to detect changes in the basal ganglia using MRI histogram in patients with CP who do not have pathological signal changes in the basal ganglia on conventional MRI images.

	ORCID No
Ferit DOĞAN	0000-0001-9507-6670
Mehmet DEMİR	0000-0002-5031-6324
Huseyin GUMUS	0000-0002-9326-2194
Celil YILMAZ	0000-0002-0951-8258

Başvuru Tarihi / Received: 20.02.2024
Kabul Tarihi / Accepted : 23.07.2024

Adres / Correspondence : FERİT DOĞAN
Harran University, Faculty of Medicine, Department of Radiology, Sanliurfa, Turkey
e-posta / e-mail : feritdogan2001@yahoo.com

Material and Method

The study population included children who were admitted to Sanliurfa Training and Research Hospital Pediatric Neurology Outpatient Clinic and had clinical features compatible with CP, such as sensory disorders accompanied by movement and posture disorders between January 2022 and June 2023. CP is a neurological disease that develops in the childhood age group and involves movement control, posture disorders, disorder of cognition, communication, perception, behavior and seizures secondary to developing brain damage. In our study, 40 patients and 60 control groups were included. When post hoc power analysis was performed, power=0.99 was found when alpha=0.05 and effect size 1.157 were taken. (Gpower 3.1 software was used.)

Inclusion criteria

Children aged>2 years with non-progressive posture or movement disorders due to a lesion in the brain during the prenatal, perinatal, or postnatal period, who were diagnosed with CP. A group of patients with normal basal ganglia and thalamus despite white matter involvement on conventional MRI was included.

Exclusion criteria

Cases with neurodegenerative disease, brain tumor, psychomotor retardation due to genetic causes, movement disorders caused by muscle or peripheral motor neuron disease, brain abscess, hydrocephalus, meningitis (both septic and tuberculous), and encephalitis.

MRI examination and histogram analysis

All patients participating in the study underwent brain MRI. All the brain MRI scans were performed on a 3T unit (Siemens Magnetom Skyra, Erlangen, Germany) using a head coil. T1, T2, T2 tirm TRA dark-fluid sequences were acquired. The T1 se tra sequence was TR: 370 ms and TE: 11 ms. The T2 se tra sequence was TR: 4540 ms and TE: 109 ms. The T2 tirm TRA dark fluid sequence was TR: 9140 ms and TE: 81 ms.

The images of 40 children with CP and 60 children with no significant intracranial findings on brain MRI examination were retrospectively evaluated. The collected MRI images were then reviewed using “Radiant DICOM Viewer 2020.2.3” software.

For image analysis, a single observer, (M.D.) with 10 years of experience in radiology, evaluated the axial slice brain MRI images of each case using the same window settings (window level 20 and window width 380). The axial image showing the basal ganglia was identified and registered. The registered images were then opened using “qMaZda v4.6” software.

The histogram parameters of mean, variance, skewness, kurtosis, 1st percentile (P), 10th P, 50th P, 90th P and 99th P were calculated for each patient and control group over the areas identified in the head of the thalamus, lentiform nucleus and nucleus caudatus and these were evaluated separately for each case (Figure 1).

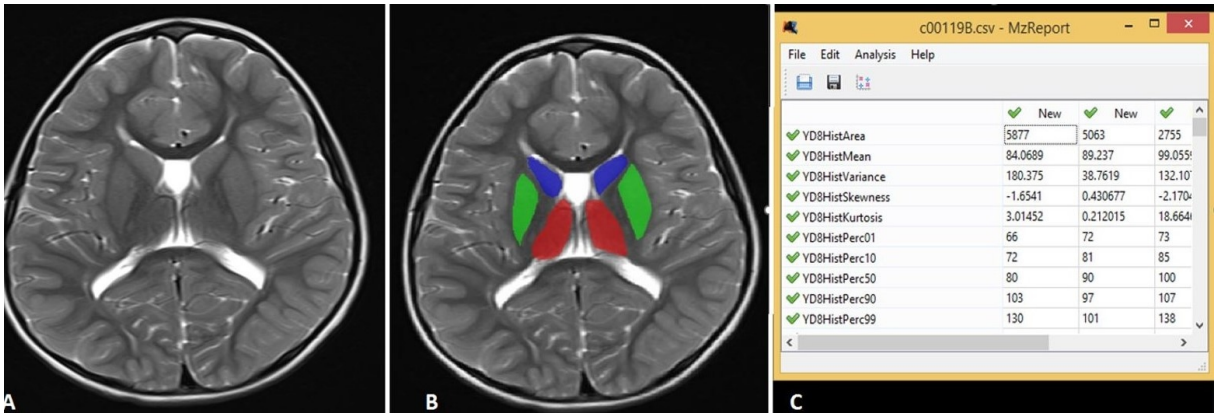

Figure 1. 5-year-old male patient with cerebral palsy. (A) Ventricular level on T2-weighted axial brain MRI image. (B) Two-dimensional segmentation of the thalamus (RED), lentiform nucleus (GREEN) and head of the nucleus caudatus (BLUE) from the same level using qMazda V.6 software. (C) Quantitative values of the histogram parameters of the area determined in image B.

Approval for this study was granted by the Harran University Medical Ethics Committee (decision no: 23.23.32, dated: 11.12.2023). All the study procedures were in compliance with the Declaration of Helsinki.

Statistical analysis

Statistical analyses were performed using SPSS version 22.0 software (IBM Inc, Armonk, NY, USA). The conformity of numerical data to normal distribution was assessed with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistics were stated as mean±standard deviation

values for numerical data showing normal distribution, and as median with minimum-maximum values for numerical data not showing normal distribution. The Independent Student's t-test and Mann Whitney U-test were used for intergroup comparisons. A value of $p<0.05$ was considered statistically significant.

Results

The images of 40 children with CP and 60 children in the control group were evaluated. The CP group comprised 22 boys and 18 girls with a mean age of 7.58±3.45 years, and the control group comprised 35 boys and 25 girls with a mean age of 8.1±2.48 years. No significant difference was found between the patient and control groups in terms of age and gender (p=0.410, p=0.742, respectively) (Table 1).

In the brain MRI images of the patient and control groups, histogram analyses were performed from the thalamus, lentiform nucleus and nucleus caudatus. A significant difference was determined between the groups in respect of the mean, kurtosis and 50th P values of the histogram parameters obtained from thalamus (p=0.001, p=0.002, p=0.025, respectively) (Table 2). In the measurements made in the thalamus, mean and 50th p values were found to be low and kurtosis value was found to be high in CP patients.

Table 1. Age and gender distribution of the patient and control groups.

	CP (n=40)	Control (n=60)	p
Age	7.58±3.45	8.1±2.48	0.410[a]
Sex			
Male, n (%)	22 (55)	35 (58.3)	0.742[b]
Female, n (%)	18 (45)	25 (41.6)	

[a]Independent samples T Test. [b]Pearson Chi square test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or number (%).

Table 2. Histogram parameters and comparison of images obtained from Thalamus in patients and control group.

	CP (n=40)	Control (n=60)	p
Mean	78.7±10.2	89.4±10.1	**0.001[a]**
Variance	39.1±11.2	41.1±12.1	0.195[a]
Skewness	-0.15 (-1.1 - 0.13)	-0.11 (-1 - 0.16)	0.085[b]
Kurtosis	-0.388 (-0.12 - 0.62)	-0.50 (-0.32 - 0.81)	**0.002[b]**
1th P	60.2±9.5	62.2±9.41	0.123[a]
10th P	68.9±10.5	74.2±9.1	0.069[a]
50th P	79.8±10.2	88.5±9.5	**0.025[a]**
90th P	91.2±11.5	96.5±10.1	0.065[a]
99th P	97.2±10.1	101±11.2	0.089[a]

[a]Independent samples T Test. [b]Mann-Whitney U test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or median (minimum - maximum).

A significant difference was found between the mean, skewness, kurtosis and 1st P values of the histogram parameters obtained from the lentiform nuclei (p=0.021, p=0.005, p=0.015, p=0.035, respectively) (Table 3). In the measurements performed in the lentiform nuclei, mean, skewness and 1st p values were found to be low and kurtosis value was found to be high in CP patients.

A significant difference was found between the mean, kurtosis, 90th P and 99th P values of the histogram parameters obtained from the head section of the nucleus caudatus (p=0.002, p=0.03, p=0.004, p=0.042, respectively) (Table 4). In the head section of the Nucleus Caudatus mean, 90th P and 99th P values were found to be low and kurtosis value was found to be high in CP patients.

Table 3. Histogram parameters and comparison of images obtained from Lentiform Nucleus in patients and control group.

	CP (n=40)	Control (n=60)	p
Mean	75.6±9.8	84.5±10	**0.021[a]**
Variance	45.2±12.2	40.5±11.8	0.320[a]
Skewness	-0.3 (-0.51 - 0.21)	-0.11 (-0.31 - 0.8)	**0.005[b]**
Kurtosis	-0.3 (-0.4 - -0.11)	-0.45 (-0.78 - -0.25)	**0.015[b]**
1th P	61±8.5	69±9.2	**0.035[a]**
10th P	66.2±10.1	74.2±8.9	0.089[a]
50th P	75.2±8.2	83.1±8.8	0.075[a]
90th P	88.9±10.2	96±10.3	0.065[a]
99th P	100±9.8	101±11.2	0.165[a]

[a]Independent samples T Test. [b]Mann-Whitney U test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or median (minimum - maximum).

Table 4. Histogram parameters and comparison of the images obtained from the head section of the Nucleus Caudatus in the patient and control groups.

	CP (n=40)	Control (n=60)	p
Mean	77.6±9.6	88±10.1	**0.002**[a]
Variance	42.4±11.8	39.4±10.1	0.252[a]
Skewness	-0.15 (-0.31 – 0.1)	-0.14 (-0.28 – 0.11)	0.075[b]
Kurtosis	-0.49 (-0.82 – -0.12)	-0.72 (-1.1 – -0.32)	**0.030**[b]
1th P	63±7.7	66±8.1	0.082[a]
10th P	67.1±9.9	72.1±8.9	0.078[a]
50th P	78.1±7.9	8.2±7.2	0.120[a]
90th P	82.2±12.1	97.2±11.2	**0.004**[a]
99th P	95.4±9.7	103±13.1	**0.042**[a]

[a]Independent samples T Test. [b]Mann-Whitney U test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or median (minimum - maximum).

Discussion

This study, using tissue analysis, also revealed effects at the lentiform, caudate nucleus and thalamus levels of patients with CP, which cannot be visually detected with conventional MRI.

Genetic and metabolic causes should be investigated in CP patients whose history is not clear or in whom atypical clinical features are observed. In cases where etiology cannot be determined, MRI, which is considered the most predictive tool, is used to detect risk (10).

Traditional and advanced techniques have been described regarding brain MRI findings in children with CP (11). Histogram-based statistics, an advanced technique, measure the global distribution of pixels/voxels of gray level tones (12–14). The MRI findings have been reported to be abnormal in 86% of CP cases. Periventricular white matter damage is the most common finding at the rate of 56%, followed by deep gray matter damage at 18% (9). This study is the first to have investigated whether the basal ganglia are involved in CP patients with white matter involvement using MRI histogram analysis.

Quantitative imaging features can be derived from MRI-based texture analysis (TA), encompassing a variety of characteristics. The first-order statistical feature, often referred to as a histogram, involves the distribution of voxel densities within the region of interest. This distribution is based on fundamental properties such as skewness, kurtosis, entropy, and energy of grey level density. Based on the TA results of the patient and control groups in the current study, these differences were thought to be an indicator of heterogeneity in the brain parenchyma of CP patients (15). Statistical calculations can be made from the histogram. The mean gives the average intensity level of the image, variance gives the roughness of the image, skewness defines the symmetry of the histogram, and kurtosis defines its flatness (16).

Sarıoglu et al. (15) made this possible by using MRI-based TA of the basal ganglia and thalamus for the accurate diagnosis of moderate to severe hypoxic ischemic encephalopathy in newborns. TA may provide objective features that can reveal visually undetectable MRI differences in the basal ganglia and thalamus of perinatal asphyxiated newborns. Wang et al. (17) reported that histogram analysis would be useful in the demonstration of hypoglycemic encephalopathy in the neonatal period. Suoranta et al. (16) performed 3D TA of bilateral thalamus, amygdala, hippocampus, caudate nucleus and putamen of 16 patients with progressive myoclonic epilepsy type 1 and 16 healthy control subjects. There were reported to be significant textural differences in progressive myoclonic epilepsy type 1 patients compared to the control group, especially in the thalamus and right putamen. Valdés et al. (18) suggested that basal ganglia TA can be used to evaluate blood-brain integrity in small vessel disease. The results of the current study showed that patients with CP had lower mean values in the thalamus, lentiform and caudate nuclei than the control group. This demonstrated lower tissue density in the thalamus, lentiform and caudate nuclei in patients with CP than in healthy control subjects.

The current study patients with CP had higher kurtosis values in the thalamus, lentiform and caudate nuclei than the control group. This showed that the flatness of the thalamus, lentiform and caudate nucleus tissue in patients with CP was greater than in the healthy control subjects.

The patients with CP were found to have lower skewness values in the lentiform nucleus than the control group, thereby demonstrating lesser histogram symmetry of the tissue in the lentiform nucleus in patients with CP than in the healthy control group.

Baykara et al. (19) demonstrated significant differences between patients with functional neurological disorder and healthy control subjects using histogram analysis of the amygdala. Johns et al. (20) found that basal ganglia tissue properties differ significantly in patients with amyotrophic lateral sclerosis. Bhattacharya et al. (21) compared the changes in corpus callosum in progressive supranuclear palsy using three different tissue analyses using T2-weighted MRI. These were gray level co-occurrence matrix, local binary pattern, and oriented Gaussian derivative filter-bank. It was hypothesized that progressive supranuclear palsy may cause non-selectable loss of tissue structure of

the corpus callosum. The results of that study revealed that local binary pattern TA was superior to other TA methods.

The primary limitation of this study was the retrospective design. A second limitation was that sequences may have variability in non-normalizable parameters, such as TR and TE values. There is a need for further studies to be conducted with different protocols to confirm these results. However, as there has been no similar study before, the results of this study can be considered of value in contributing to the literature. In addition, TA application is both simple and applicable to many imaging modalities.

Conclusion

Texture analysis can produce objective features that may indicate differences in the basal ganglia and thalamus in patients with CP with white matter involvement. The results of this study showed many statistically significant tissue parameters between the healthy control group and the patients with CP in the lentiform, caudate nucleus and thalamus.

Conflict of interest statement

There is no conflict of interest in our study.

Ethics Committee Approval: Approval was obtained from the Harran University Medical Ethics Committee (decision no: 23.23.32, dated: 11.12.2023).

Funding: No funding.

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