Alteration of Cerebral Blood Flow values in children with cerebral palsy using 3D pseudocontinuous Arterial Spin Labeling: Its correlation with DTI metrics.

B. Roy[1], V. Paliwal[2], P. Goel[3], S. Kumar[1], R. K. Rathore[4], S. Verma[4], and R. K. Gupta[1]

[1]Department of Radiodiagnosis, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India, [2]Department of Neurology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India, [3]Department of Anaesthesiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India, [4]Department of Mathematics & Statistics, Indian Institute of Technology, Kanpur, Kanpur, Uttar Pradesh, India

Introduction: Cerebral Palsy (CP) is caused by abnormal development or damage to one or more parts of the brain that controls muscle tone and motor activity, consequently physical disability in development, dystonia, mental retardation and epilepsy. It may occur during pregnancy, childbirth or after birth up to about age of three years. These patients may have abnormal neuroradiological findings mainly involving periventricular white matter. An immature cerebral autoregulation or a vulnerability of the autoregulation exposed by hypoxia or ischemia may be considered as main factors responsible for the changes in cerebral blood flow (CBF) autoregulation in acute phase of injury. Over the years, many advanced imaging techniques such as diffusion tensor imaging (DTI) and diffusion tensor tractography have been performed in these children and reports significant changes in DTI metrics over various brain regions (1). Decreased or normal CBF has been reported in CBF in these patients with CP by using xenon-133 inhalation single photon emission CT (2); however no study is available which quantifies CBF in these patients by MRI or CT perfusion. Arterial spin labeling (ASL) uses magnetic labeling of protons in blood to provide an endogenous tracer of flow and is a noninvasive technique that quantifies CBF in vivo (3). A number of studies are available in the literature those describe the application of ASL based CBF estimation and health and disease (4). The aim of this study was to see the changes in CBF value along with the DTI derived metric and see the correlation between CBF values and DTI derived metrics in various brain regions.

Materials and Methods:

MR Imaging: Twelve CP children with age ranging from 3-10 years were clinically assessed and included in the study. All these children had GFMS score between 50-60 and had no mental retardation or had history of seizures. Five age/sex matched controls were also included in the study. Conventional MRI, DTI and 3D pseudo-continuous arterial spin labelling (PCASL) were performed using 3T MR scanner (Signa Hdxt, General Electric, Milwaukee, USA) after the approval from the institutional ethics committee. DTI data were acquired using dual spin-echo single-short echo-planar sequence with ramp sampling with 30 uniformly distributed directions. The acquisition parameters were: TR= 10sec/ TE= 100ms/ slice no. = 46/ thickness =3mm/ interslice gap= 0/FOV= 240mm/ image matrix = 256*256 /NEX =1/ diffusion weighting b-factor = 1000s mm^{-2}. PCASL was performed using the following parameters: Frequency =512/ Phase= 8/ NEX =3/ no. of slices = 46/ FOV= 24/ slice thickness = 3mm/ band width =62.5 on the same locations as was used for DTI and conventional MRI. DTI data was processed by using JAVA based in-house developed DTI-software (5). The DTI metrics and CBF maps were co-registered using mutual information (6). Regions of interest (ROIs) were placed for obtaining mean diffusivity (MD), FA and CBF values simultaneously in various white matter and grey matter regions (fig 1-D).

Statistical Analysis: For the purpose of comparison of DTI derived metrics and CBF value between controls and patients Mann-Whitney rank sum test was performed. Spearman's correlation was performed to look whether any of the DTI metrics were significantly correlated with the CBF values.

Results: On ASL, CP children showed significantly increased CBF in 7/10 white matter regions; frontal white matter (FWM), anterior limb of internal capsule (ALIC), posterior limb of internal capsule (PLIC), genu, splenium, parietal white matter (PWM) and occipital white matter (OWM) as compared to controls; however only one region in gray matter showed significantly increased CBF as compared to controls (table1). These patients showed significantly decreases FA value in all regions with increased CBF values (table 2). Few regions of the brain showed significant negative correlation between CBF and FA value such as caudate nuclei (r= -0.685, p= 0.014), ALIC (r= -0.804, p= 0.002) and OWM (r= -0.706, p=0.01).

Regions	Control	Patients	P value
FWM	18.99±7.48	35.06±07.43	0.008
ALIC	33.30±6.08	49.54±10.33	0.004
PLIC	16.56±3.80	30.06±13.69	0.015
Genu	18.79±3.21	42.61±16.21	0.006
Splenium	25.73±5.95	47.51±19.66	0.015
PWM	32.92 ±13.8	57.31±10.84	0.002
OWM	19.75±5.90	46.68 ±11.51	0.002
FGM	43.30±12.1	62.74±17.71	0.020

Table 1: Summary of CBF (ml/100g/min) values of different brain regions of CP patients and controls.

Regions	Control	Patients	P value
FWM	0.48±0.13	0.32±0.07	0.020
ALIC	0.51±0.09	0.30±0.06	0.002
PLIC	0.62±0.04	0.42±0.07	0.002
Genu	0.70±0.07	0.44±0.14	0.002
Splenium	0.81±0.04	0.46±0.09	0.002
PWM	0.38±0.05	0.22±0.06	0.002
OWM	0.63±0.10	0.29±0.07	0.002

Table 2: Summary of FA values of different brain regions of CP patients and controls.

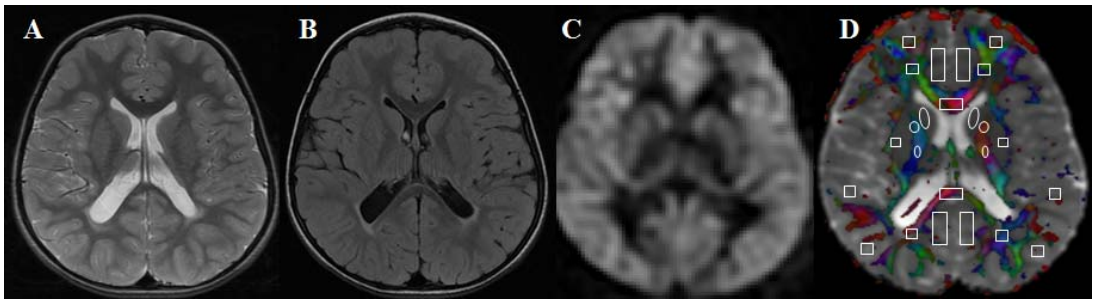

Fig 1: A. T_2 weighted, B, T2 FLAIR images show minimal hyper intensity in the periventricular regions. C. CBF map of a CP child with spastic diplegia. D. showing the co-registered map of CBF with DTI metrics and region of interest placed in different brain regions at the level of third ventricle

Discussion: In this study we observed significantly increased CBF and decreased FA value in few brain regions as compared to controls. CBF showed significant negative correlation with FA values in CN, ALIC and OWM. Increased CBF has been reported in acute hypoxic injury and stroke using ASL technique (7). It appears that the increased CBF values in the various white matter regions which also show decrease FA is probably due to the compensatory response to the hypoxic damage over a period of time to attempt to maintain some functionality. This can also be seen by the negative correlation between FA values and CBF in some of the white and grey matter regions. Our study suggest that the CBF may be used as a marker for brain plasticity and may be of value in assessing the therapeutic response to various interventions used in these CP patients.

Reference: (1) Trivedi R et al. Pediatric Neurol 2008; 39:341-349. (2)Taudorf K et al.Neuropediatrics 1989; 20: 33-40 (3) Sourbron S. Eur J Radiol.2010 [Epub ahead of print]. (4)Wolf RL et al. Neurotherapeutics 2007; 4: 346-59. (5) Purwar A, et al. Proceedings of ESMRMB, 2006, 21-23, Abstract #644. (6) Verma, et al.2008 ESMRMB, 25th Annual Meeting, Valencia. (7) Pollock JM et al. Am J Neuroraddiol 2008; 29: 1302-1307.