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Early developmental changes in the brain: A case study on infant using ^{18}F-FDG PET

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Abstract
Brain undergoes most of the dynamic change in utero and the developmental changes continue over the first two postnatal years of life. Early phase of life is very crucial as neurodevelopmental disorder such as Autism, ADHD are likely to be noticeable during the first years of life. Better understanding of normal brain pattern is necessary for identifying abnormal developmental pattern. In the present case, a typical neurologically normal infant was scanned using ^{18}F-FDG PET during its sixth and ninth months. At sixth month, infant showed maximum ^{18}F-FDG uptake in subcortical structures including basal ganglia and thalamus. After three months follow-up from the baseline the infant showed increased ^{18}F-FDG uptake globally. Basal ganglia, thalamus and visual cortices showed maximum ^{18}F-FDG uptake compared to other regions of the brain, while medial temporal cortex and cerebellum showed the minimum ^{18}F-FDG uptake. The present case demonstrates the brain ^{18}F-FDG uptake in an infant and showed a pattern of development over a period. Infant brain ^{18}F-FDG uptake changes throughout childhood and was not restricted to early postnatal years. Moreover, the present case report helps in determining the pattern of abnormalities associated with basal ganglia and thalamus.

Keywords: ^{18}F-FDG PET, Infant, basal ganglia, thalamus, brain

1. Introduction
Brain undergo most of the dynamic change in utero and the developmental changes continue over the first two postnatal years of life. During this period of postnatal life, there is a dramatic increase in the overall size of the brain, formation of new synapses corresponding to the overall increase in grey matter volume and rapid myelination of white matter tracts and fibres [1-3]. Further, neurodevelopmental disorder such as Autism, ADHD are likely to be noticeable during the first years of life as a result of abnormal changes in early brain development. Therefore, definite understanding of normal neuronal mechanism is necessary for identifying abnormal developmental pattern in infants.
Molecular neuroimaging techniques such as Positron emission tomography (PET) has emerged as a non-invasive test to detect abnormalities in the chemical functions and/or receptor expression at the cellular level. The advancement in the quantification and techniques enable PET to detect pathological and functional changes even before the onset of clinical symptoms.^{18}F-FDG (fluorodeoxyglucose) is the most common and widely used tracer in PET, and the signal reflects astrocyte/neuron coupled energy consumption [4]. In the present case, a typical neurologically normal infant was scanned using ^{18}F-FDG PET during six and nine months.

2. Case presentation
The infant was referred for Whole body PET/CT examination for oncological evaluation. The infant was selected with a certain inclusion criteria 1. Absence of any central nervous system metastases, 2. Absence of any neurological condition such developmental abnormalities, epilepsy and infections 3. No usage of antiepileptic medication or other medication which directly affect the glucose metabolism in brain. The brain region was isolated from vertex to toe of a whole body PET/CT images and then processed. The brain ^{18}F-FDG PET images were normalized and aligned using ADW software by GE for visual interpretation.

3. Result
During sixth month scan, infant showed maximum ^{18}F-FDG uptake in subcortical structures including basal ganglia and thalamus. Partially increased ^{18}F-FDG uptake was observed in some parts of middle and superior frontal cortex, and middle cingulate cortex. Except for the regions mentioned above other cortical and subcortical regions showed reduced ^{18}F-FDG uptake (Fig.1).

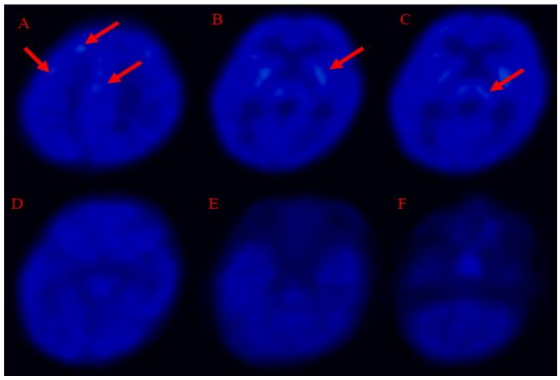

Fig 1: Schematic representation of Transaxial ^{18}F-FDG PET brain image of an infant during six months. Globally ^{18}F-FDG brain uptake was observed low, except few regions. (A) Some part of superior and middle frontal cortex along with middle cingulate gyrus showed comparatively greater ^{18}F-FDG uptake. (B) Subcortical structures including basal ganglia and thalamus show maximum ^{18}F-FDG uptake.

Three month of follow-up from the baseline, increased ^{18}F-FDG uptake was seen globally. Basal ganglia, thalamus and visual cortices showed maximum ^{18}F-FDG uptake compared to other regions of the brain. While, medial temporal cortex and cerebellum showed the minimum ^{18}F-FDG uptake (Fig 2).

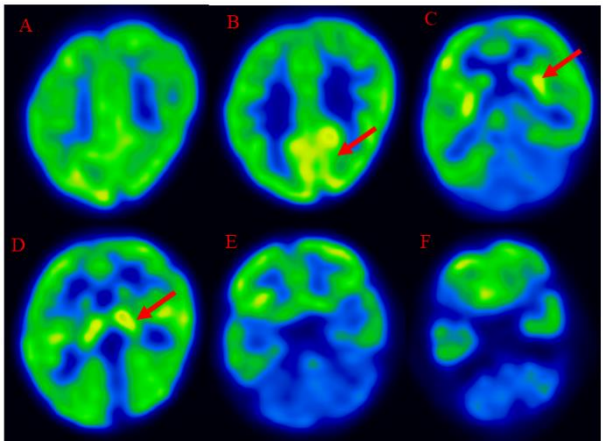

Fig 2: Schematic representation of Transaxial ^{18}F-FDG PET brain image of an infant during nine months. Globally ^{18}F-FDG brain uptake was increased. Increased ^{18}F-FDG was noted in visual and surrounding cortices (B), basal ganglia (C), and thalamus (D). Cerebellum (F), and medial temporal cortex (E) show comparatively lower ^{18}F-FDG uptake as compared to other regions of the brain.

4. Discussion

In this case study, we delineated the development of the brain pattern using ^{18}F-FDG PET during the first six months of postnatal years along with a follow-up period of three months. Few neuroimaging studies using ^{18}F-FDG PET have been studied to describe early neuronal changes in neonates and correlated with future clinical findings [5-7]. Earlier ^{18}F-FDG PET studies on infants showed highest ^{18}F-FDG uptake in sensory motor cortex, thalamus and brainstem by two months, and thereby increased ^{18}F-FDG uptake noted in frontal, temporal, parietal, occipital cortices and cerebellar cortices by five months [8]. In contrast to earlier studies, we observed globally reduced ^{18}F-FDG uptake in cortex during first six months of postnatal years. Basal ganglia and thalamus showed maximum ^{18}F-FDG uptake during this period. This could be associated with the early establishment of thalamic cortical connectivity pattern in the brain. The increase in the basal ganglia might probably due to the development of higher order motor control function. Moreover, previous case studies on perinatal hypoxia showed hypermetabolism (increased ^{18}F-FDG uptake) in basal ganglia and later developed dystonic cerebral palsy [5]. However, in the present case both basal ganglia and thalamus showed similar ^{18}F-FDG uptake. The present case report gives a better comprehension on classifying normal brain development from hypoxia. Further studies on subcortical brain regions are necessary for a better understanding of the physiology of the brain development.

During the ninth month scan, the infant showed increased ^{18}F-FDG uptake in the frontal, temporal and parietal cortices as compared to baseline scan. The present case was in agreement with the previous studies showing increased ^{18}F-FDG uptake in frontal and association cortices between eight to nine months [9]. This increased ^{18}F-FDG uptake could be due to both increase in the capillary density and expansion of dendrite fields [10]. Moreover, basal ganglia, thalamus and visual cortex showed the maximum ^{18}F-FDG uptake during ninth month scan as compared to other regions of the brain. This maximum ^{18}F-FDG uptake in the visual cortex might possibly be related with the increased synaptogenesis in the visual cortex during eight months to two years [11]. In addition, cerebellar cortex and medial temporal cortex showed the lowest ^{18}F-FDG uptake. Cerebellum was one of the first structure in the brain to begin differentiation and last to mature, and this could possibly be associated with lower metabolism as compared to other regions [12]. This also might be due to the different cellular organization of the cerebellum which changes continually many months after birth [12]. Also, lower ^{18}F-FDG uptake in medial temporal cortex could be related with the later stage of maturational development in infants.

However, in the present case infant brain ^{18}F-FDG uptake did not resemble like a young adult brain pattern as previously shown by Chugani [13]. This signifies that regional ^{18}F-FDG uptake changes throughout childhood, and suggesting that infant's brain had not reached adult pattern in its first year of life [14]. The present case also brings to the notice that during six to nine months the maturation of the brain take place globally.

Although, the present case provides detailed information regarding the developmental mechanism of an infant brain, it still had some limitations. Due to ethical issues, ^{18}F-FDG-PET on healthy infant was not possible. The infant who had come for oncological evaluation and follow-up data was studied. Long term follow-up of the infant was not available.

In summary, the present case demonstrates the brain ^{18}F-FDG uptake in an infant and showed a pattern of development over the first postnatal year. Basal ganglia, thalamus and visual cortex regions showed maximum ^{18}F-FDG uptake during nine months, while cerebellum and medial temporal cortex showed the minimum ^{18}F-FDG uptake. Infant brain ^{18}F-FDG uptake changes throughout childhood. Moreover, the present case report helps in determining the pattern of abnormalities associated with basal ganglia and thalamus in the early postnatal years.

5. Conflict of interest

Author(s) declare no conflict of interest

6. Reference

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