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Short Commentary

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Atlas of 99mTc-HMPAO SPECT brain perfusion in pediatric brain disorders

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Abstract

Background: Blood flow to the brain is in parallel with brain metabolism in almost all brain disorders except in brain tumors and therefore regional cerebral blood flow can be used as a marker of metabolic brain activity and hence it is closely linked to neuronal activity, the activity distribution is presumed to reflect neuronal activity levels in different areas of the brain.

Purpose: The aim of this work is to demonstrate to pediatrician in general and pediatric neurologist in particular the variations in cerebral perfusion during normal development which should be taken into consideration at the time of interpreting SPECT brain perfusion scan in different pediatric brain disorders.

Method: Brain SPECT was performed 10 minutes after an intravenous injection of 11.1 MBq/kg (0.3 mCi/kg), and the minimum dose is 185 MBq (5 mCi) of 99mTc-HMPAO (4).

Results: This was a retrospective analysis of SPECT brain perfusion scan of pediatric patients performed between October 2015 and December 2019 at our institution. We selected normal and abnormal studies in pediatric population with age range (5 months - 14 years).

Conclusion: Although anatomic cross sectional imaging give details of neurological structural changes, SPECT perfusion mirrors indirectly both metabolic and neuronal activity changes. Therefore, accurate interpretation of SPECT perfusion will consolidate its role as part of the diagnostic protocol and used when the findings of other imaging modalities do not explain the symptoms or fail partially or completely in determining the etiology of brain disorders in pediatric patients.

Keywords: Blood; Brain disorders; Tumors; Cerebral blood flow; Injection.

Abbreviations: ADHD: Attention Deficit Hyperactivity Disorder; MMD: Moyamoya Disease; RCBF: Regional Cerebral Blood Flow; SPECT: Single-Photon Emission Computed Tomography; 99mtc-HMPAO: Technetium-99m-Hexamethylpropyleneamine Oxime; 99mtc-ECD: 99mtc-Ethylene Cysteine Diethylester.

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Background

Blood flow to the brain is in parallel with brain metabolism in almost all brain disorders except in brain tumors and therefore regional Cerebral Blood Flow (rCBF) can be used as a marker of metabolic brain activity [1] and hence it is closely linked to neuronal activity, the activity distribution is presumed to reflect neuronal activity levels in different areas of the brain. Furthermore, (rCBF) has been described to reflect brain development and can be used to assess behavior changes in early childhood [2].

Brain perfusion can be assessed with different techniques including Nuclear Medicine (NM) Imaging and MRI studies. Single-Photon Emission Computed Tomography (SPECT) Imaging is a functional nuclear imaging technique performed to evaluate (rCBF). The most commonly used brain perfusion imaging agents are technetium-99m-hexamethylpropyleneamine oxime (99mTc-HMPAO) and 99mTc-ethylene cysteine diethylester (99mTc-ECD) with a half-life of 6.02 hours. Both are sensitive indicators of (rCBF) changes and can detect changes in blood flow overtime or immediately after an acute event [3].

The aim of this work is to demonstrate the variations in cerebral circulation and metabolism during normal development which should be taken into consideration at the time of interpreting SPECT brain perfusion scan performed to evaluate brain disorders in children and infants.

Materials and methods

Brain SPECT scanning to evaluate regional cerebral blood flow was performed 10 minutes after an intravenous injection of 11.1 MBq/kg (0.3 mCi/kg), and the minimum dose is 185 MBq (5 mCi) for both brain-specific agents [4]. The injection was made within 30 minutes after kit preparation.

Patients were positioned supine in supine with the head in a head holder and/or secured with a velcro strap to prevent motion. The head is flexed so that the cerebellum is included in the field of view. Imaging room should be quiet and dimly lit.

Imaging was performed using a dual head gamma rotating, large field-of view

(Philips' BrightView XCT) fitted with a low-energy and high resolution collimator. Sixty four images were acquired for 20 seconds each, during a 360° camera rotation. Each image was stored in a 64 X 64-pixel matrix. Reconstruction of the image was performed with attenuation correction, using Hanning filters to produce transverse, sagittal, and coronal images [5,6].

Results

This was a retrospective analysis of SPECT brain perfusion scan performed at our institution for pediatric patients between Oct. 2015 and December 2019.

We selected normal and abnormal SPECT perfusion studies in pediatric and children population with age range (5 months - 14 years).

Variations in cerebral circulation (Figure 1a-d) and metabolism during normal development must be taken into consideration at the time of interpreting SPECT brain perfusion scan performed to evaluate any brain disorders in children and infants [4].

In this work we will illustrate the different patterns of (rCBF) in common and rare neurological pediatric disorders.

Epilepsy

SPECT brain scan in epilepsy is the most commonly NM procedure performed in neurological disorders in children. Patients with intractable and refractory disease are amenable to surgical treatment. Those selected for surgery should have in addition to clinical examination different investigations including Electroencephalogram (EEG), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and brain SPECT to localize the epileptic focus [5,6].

The scintigraphic patterns of brain SPECT in epilepsy differ whether performed during ictal or interictal phase showing increased uptake in the former (Figure 2a) and decreased uptake in the latter (Figure 2b).

Non-epileptic causes of seizure

A non-epileptic seizure is defined as a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain due to previous brain insult [7].

Certain types of seizure disorders are likely to be associated with structural brain lesions, including tumors, infection, infarction, traumatic brain injury, vascular malformations, developmental abnormalities, and other brain pathology [8]. A cause is identifiable in less than 20% of children with seizures [9].

Patients without a provoked cause of first seizure require further evaluation. Contrast enhanced CT of the brain is useful as initial investigation. MRI can depict subtle abnormalities that may go unrecognized on CT. Refractory epilepsy requires special tests such as EEG, SPECT and PET studies. Herein we will review the different scan patterns of SPECT scan in non-epileptic secondary seizures (Figure 3a-e).

Developmental disorders

Advanced imaging techniques have provided a new horizon into a relationship between the neuronal activity and brain development disorders. SPECT brain scan was one of these promissing techniques. In this review we will show the expected patterns of SPECT in autism and Attention Deficit Hyperactivity Disorder (ADHD).

Autism: Autism is a developmental disorder of an early onset characterized by deficits in verbal and nonverbal language, social skills, cognitive ability and an abnormal behavior [11]. Some SPECT studies in young children using 99m-Tc HMPAO revealed abnormal rCBF in frontal and temporal cortices [10, 11]. Figure 2a is a SPECT brain scan of a 5-year-old boy with developmental delay and autism.

Attention deficit hyperactivity disorder (ADHD) is a developmental disorder characterized by a neurobehavioral syndrome with an onset in childhood. 99mTc HMPAO brain SPECT findings at rest and during intellectual stress in children and adolescents revealed decreased perfusion in the prefrontal cortex with intellectual stress [12]. Figure 2b is a SPECT brain scan of a 4 year old intellectually stressed child diagnosed with ADHD.

Brain death

The diagnosis of brain death is based on clinical and laboratory tests including EEG [13,14]. When these tests are inconclusive, SPECT brain scan has recomended to confirm the clinically suspected brain death [15,22]. In addition it has been used in cases of organ donation when family members are welling to document the absent flow [23].

Figure 5 is a SPECT scan and a selected transaxial CT image of a patient with clinical brain death secondary to head trauma and the scan performed as a confirmatory test.

Mitochondrial disease

Mitochondrial disease is a multiorgan system disorder and the Central Nervous System (CNS) being the second most commonly affected [24]. The most pertinent CNS abnormalities in children with mitochondrial disorder on imaging include white and grey matter lesions, stroke-like lesions, brain and optic nerve atrophy, and calcifications [25]. Some of these lesions may remain without symptoms while others may present with stoke like symptoms or autism like symptoms. Different brain imaging modalities are used in the work up of those patients including CT, MRI, PET and SPECT scan. Because of daily availability, some of these techniques are more useful than others. SPECT brain scan is used to assess changes in rCBF caused by lesions seen on anatomic imaging in first place and to understand the pathophysiology of this disorder hence as mentioned before changes in perfusion are paralleled with changes in metabolism and neuronal activity. Figure 6 is a SPECT scan and selected MRI images of a patient with mitochondrial disease of the brain.

Vascular disorders: Moyamoya disease

Moyamoya Disease (MMD) is a vascular occlusive disease and was firstly described by T. K. Shimizu in 1957 as a "bilateral hypoplasia of internal carotid arteries" [26].

MR angiography and CT angiography are the imaging modalities currently used to assess the spectrum of vascular changes in moyamoya disease [27].

SPECT brain scan was used to assess cerebral hemodynamics in children with Moyamoya Disease [28] and to demonstrate the extent of the impaired rCBF in ischemic areas [29]. Figure 7: SPECT and MRI images of a 10 year-old boy with left sided hemiplegia due to MMD.

Brain inflammation and infections

Encephalitis refers to a diffuse brain parenchymal inflammation mainly due to viral infections. Meningitis is an inflammation of meninges surrounding both brain and spinal cord. It can be caused by viral, bacterial and fungal infections. Symptoms include headache, fever, confusion, drowsiness and fatigue, and in some cases seizures or convulsions, hallucinations, stroke, hemorrhage and memory problems may occur [30].

In acute viral encephalitis SPECT scan shows increased uptake in affected area which will be normalized or shows decreased uptake in follow up study [31].

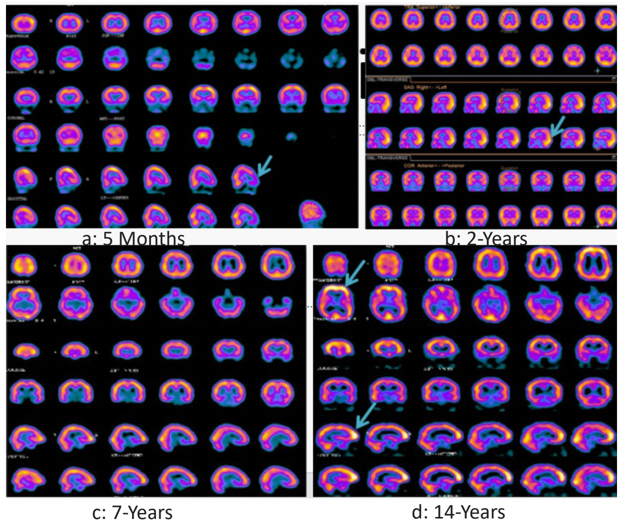

Figure 1: SPECT brain scan: Normal variation of rCBF per age: **(a)** Decreased uptake in frontal lobe (arrow) at age of 5 months. **(b)** Increased uptake in occipital lobe (arrow) and normalization in frontal lobe in a 2 year old. **(c)** Homogeneous uptake in cerebral cortex in a 7 year old. **(d)** Increased uptake in frontal lobe (arrow) in a 14 year old (adolescent age).

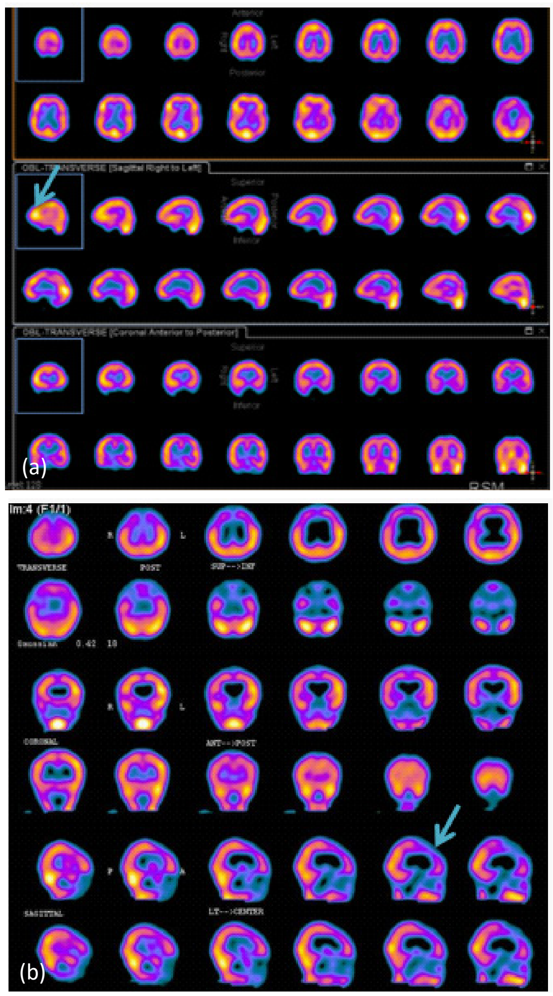

Figure 2: **(a)** SPECT brain perfusion obtained during ictal phase showing increased uptake (arrow) in right frontotemporal region (Hyperfrontality). **(b)** SPECT obtained during interictal phase showing decreased uptake (arrow) in right frontotemporal region (Hypofrontality).

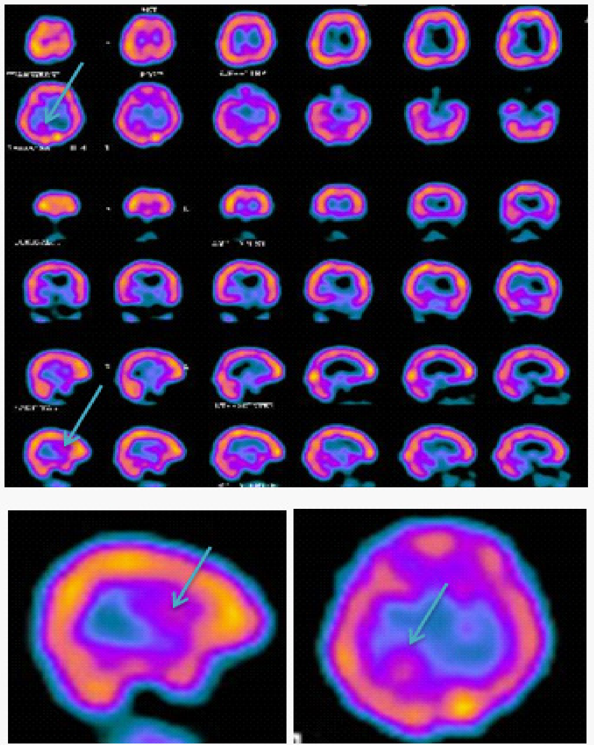

Figure 3a: Partial seizure secondary to gray matter heterotopia in a 2-year-old boy (arrows).
SPECT: Normal rCBF in both cerebral cortex. In addition, there were areas of increased uptake in the right occipital subcortical region and right fronto parietal subcortical region (arrows). The subcortical uptake was correlated with MRI (Not shown) and match with grey matter heterotopia.

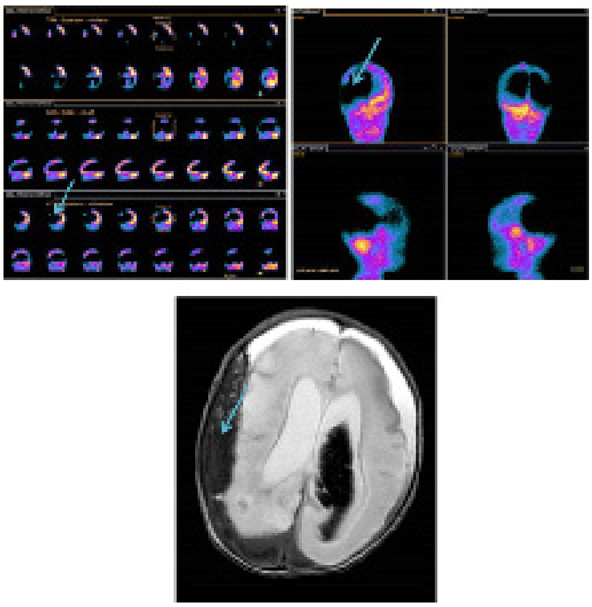

Figure 3b: Seizure post hypoxic ischemic encephalopathy (HIE) and hydrocephalus in a 1-year-old preterm boy.
SPECT and planar image (top) showed a large perfusion defect in right cerebral cortex (arrow) and smaller defect in left parietal lobe (arrow). CT (down) showed bilateral acute subdural hematoma with subarachnoid, intraventricular and intraparenchymal hemorrhage and diffuse extensive ischemic changes with cortical laminar necrosis.

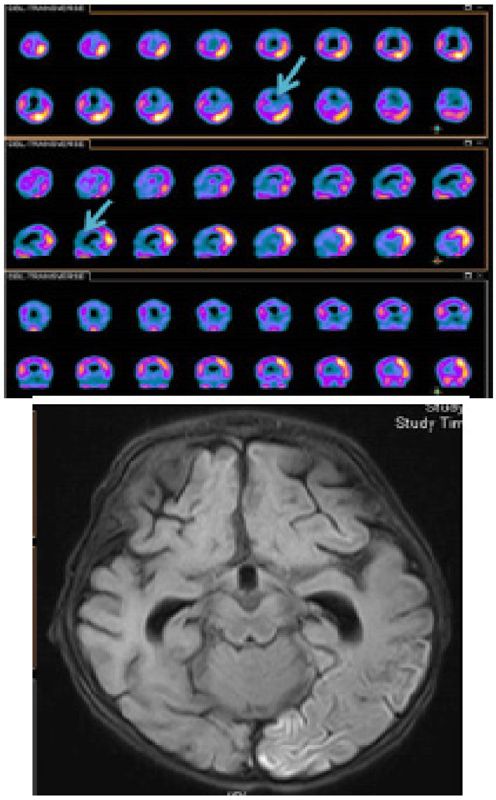

Figure 3c: Seizure post- traumatic brain injury in a 7-month male patient.
SPECT: Loss of perfusion to both frontal lobes (left affected more than right) and left temporal lobe as well(arrows).
MRI: Sequela of old ischemic insult involving mainly the left hemisphere and anterior part of the right frontal lobe associated with global brain atrophy. “Small chronic subdural hemorrhage at left frontal region and interhemispheric fissure.

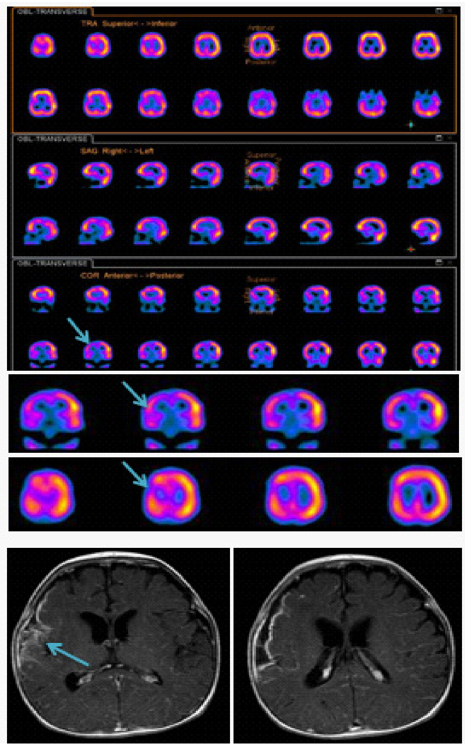

Figure 3d: A 6-month old girl is with seizures and history of meningitis.
SPECT scan :Decreased rCBF (arrows) in right frontal and right temporal lobe (upper images). MRI: Right frontotemporal meningoencephalitis (arrow) complicated with small amount overlying subdural collection (? Empyema) (Lower images)

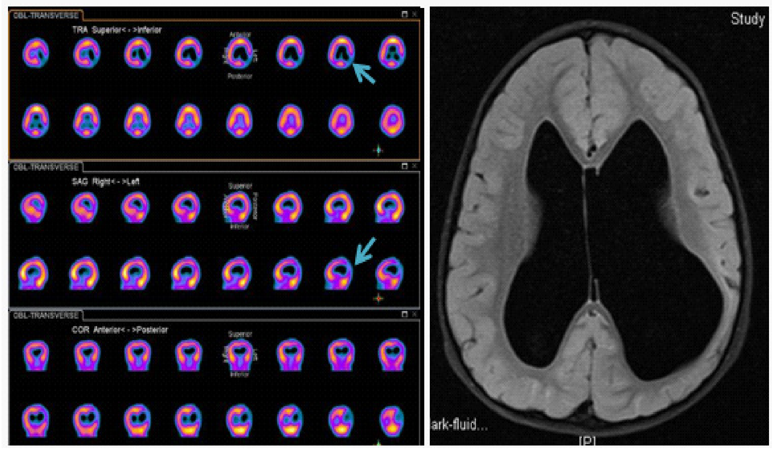

Figure 3e(1): seizure in a 3-year-old female patient with Chiarri Malformation Type II. SPECT scan: Absent regional cerebral blood flow in left parietooccipital lobe. In addition, there was decreased regional cerebral blood flow in right occipital region

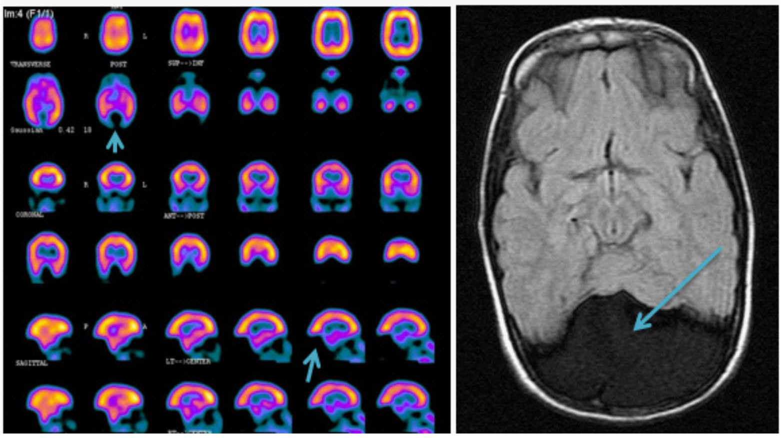

Figure 3e(2): Seizure in an 8-year-olf female patient with Dandy walker cyst. SPECT scan: Absent rCBF in cerebellum .MRI: Large posterior fossa cyst communicating with the 4th ventricle with subsequent hypoplasia of the cerebellum and small rotated vermis (arrow).

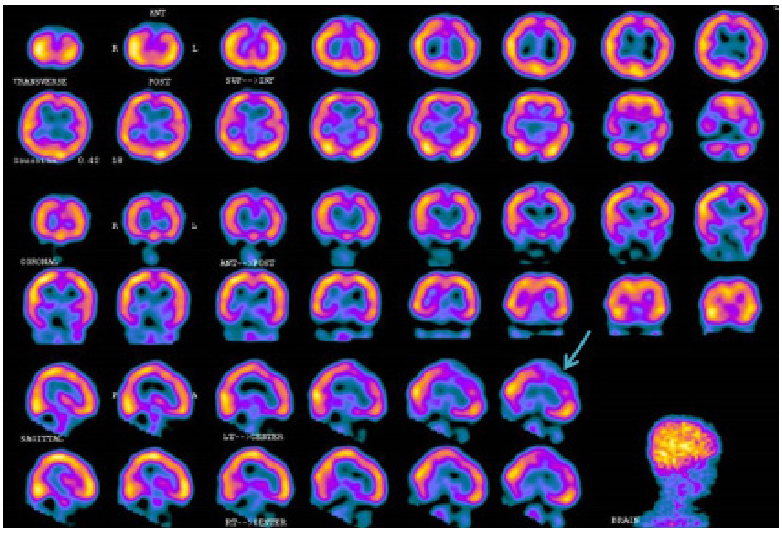

Figure 4a: A 5 years old boy is with development delayed. Patient had autism and seizure disorder. SPECT: Decreased regional cerebral blood flow in left fronto parietal region.

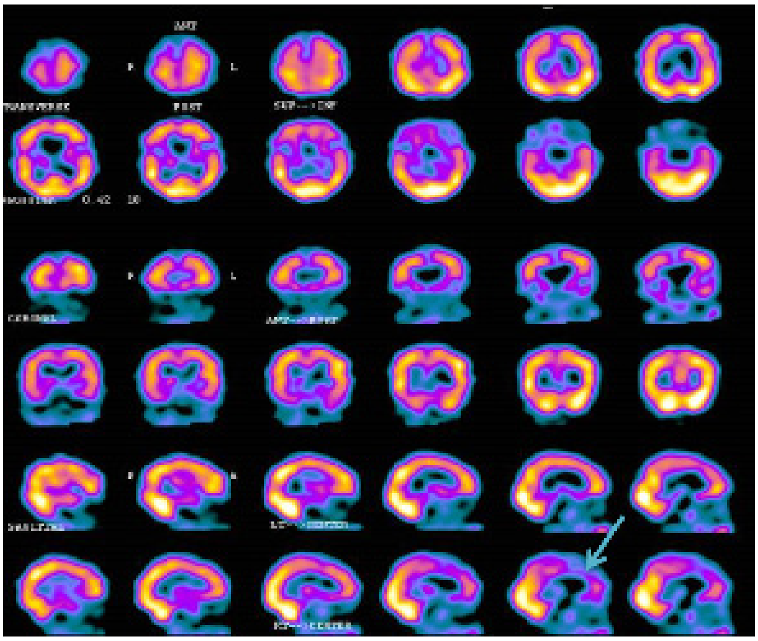

Figure 4 (b): A 10-year-old boy with ADHD.
SPECT: Severe hypoperfusion in the right orbitofrontal regions of the prefrontal cortex.

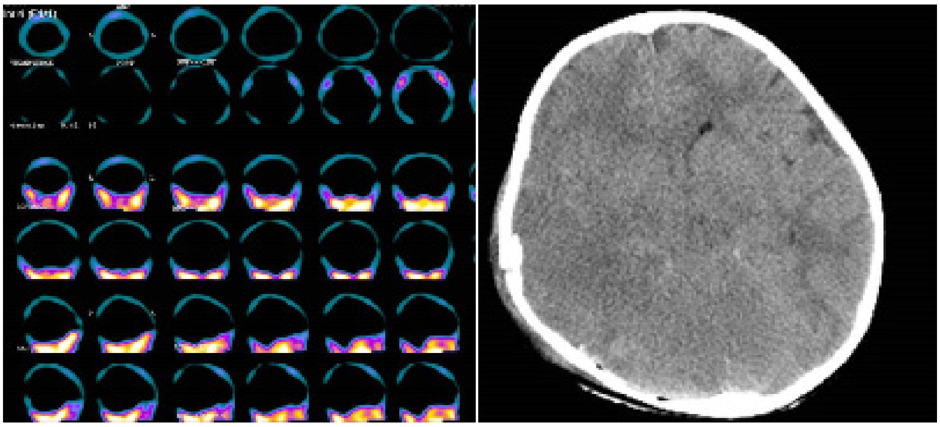

Figure 5: 3 years old girl, with head injury?. brain death.
SPECT: There was complete loss of regional cerebral blood flow with non-visualization of cerebral cortex (hollow skull).
CT: Diffuse brain edema with loss of gray/white matter differentiation.

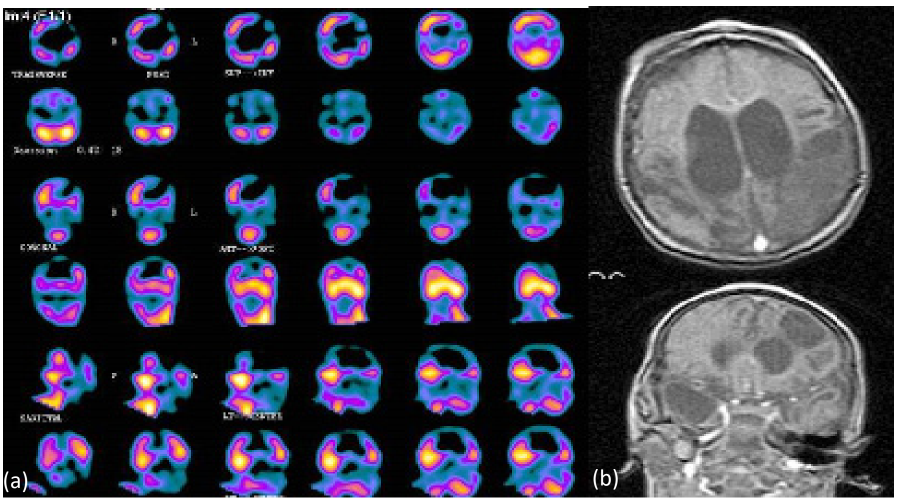

Figure 6: Mitochondrial disease in an 8-year-old girl.
SPECT **(a)**: Significant multiple perfusion cortical defects corresponding to lesions on MRI **(b)**.

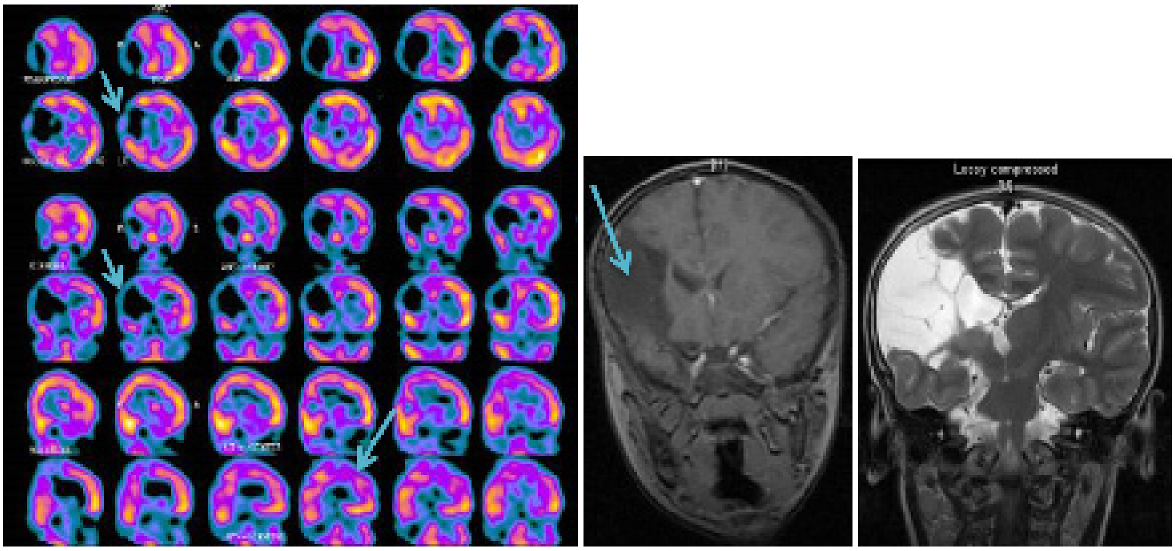

Figure 7: A 10 years old boy with left sided hemiplegia. Developmental delay and seizure.
SPECT: Large perfusion defect (arrow) involving great part of right cerebral hemisphere (fronto parietal, parieto occipital and parietal lobes) matching with MRI changes.

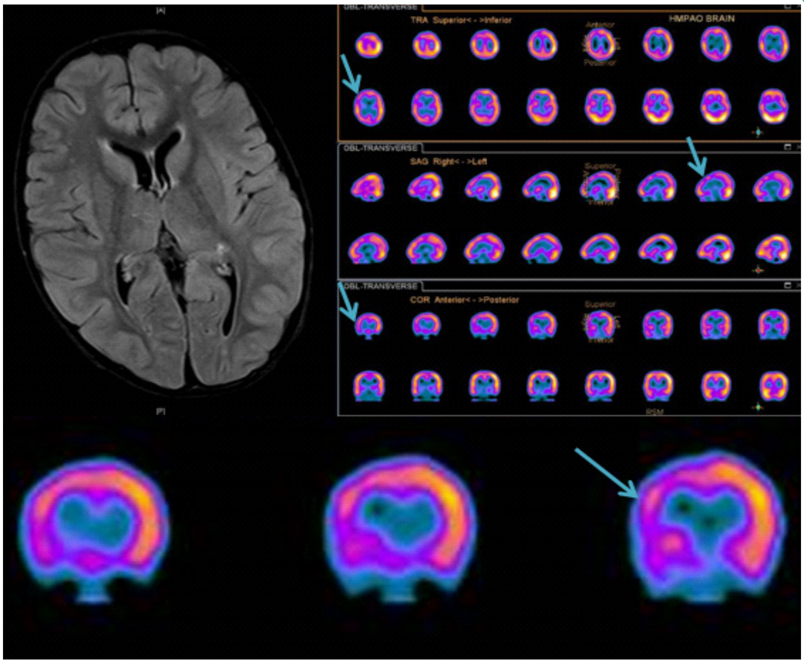

Figure 8: Viral meningoencephalitis: A 4-year-old female patient with left sided weakness. Picture of encephalitis. SPECT: Decreased regional cerebral blood flow in right frontoparietal hemisphere. Normal MRI (Not shown).

Discussion

Changes in brain function can be assessed by brain perfusion studies hence flow and metabolism are paralleled process in most brain disorders with the exception of brain tumors [1]. MRI is currently the method of choice to assess rCBF by use of Arterial Spin-Labeling (ASL) and being noninvasive and with no radiation hazard [32] which requires a specialized center and expertise. 99m-Tc HMPAO or ECD SPECT can be used to measure regional cerebral perfusion [33] and the procedure can be performed in any nuclear department. M Gervil et al [34] in a group 27 children with neurological disorders and investigated by MRI and EEG they found that SPECT brain scan added important information to 21 patients and directly led to a change in diagnosis and better assessment of the prognosis in 4 of them. They concluded that SPECT is an important imaging modality in children with brain disorders of a partially or completely unknown etiology.

Conclusion

Although anatomic cross sectional imaging give details of neurological structural changes, SPECT perfusion mirrors indirectly both metabolic and neuronal activity changes. Therefore, accurate interpretation of SPECT perfusion will consolidate its role as part of the diagnostic protocol and used when the findings of other imaging modalities do not explain the symptoms or fail partially or completely in determining the etiology of brain disorders in pediatric patients.

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