# Cerebral Vascular and Other Pathophysiology Found For High Values of SPECT or PET Derived Cerebrocortical Perfusion and Metabolic Indices

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**Abstract**

Background: New brain SPECT/PET perfusion (BPi), metabolic (BMi), or combined (BMPi) indices define normal and pathophysiologic states derived from cortical indices CMI or CPI, primarily explored to date for mixed dementia, with low CMi and CMi. Abnormally increased CPi and CMi also decreased BMPi.

Aims: Explore pathophysiology of cerebral hyperperfusion/hypermetabolism (high CPi or CMi) with new SPECT/PET indices: BMi, Bpi, and BMPi.

Methods: Labeled tracers were injected in a quiet, dark room before or after perfusion stimulants. CPi or CMi were ratios of activity within 60% to 30% supratentional isocontours; white matter indices, WMi and WPi used the (30% - 60%) to 30% isocontour activity ratio. For b=cerebral ventricular activity as a % peak brain activity (usually 20%), BMi=(CMi)(WMi)/b, BPI=(CPi)(WPi)/b and BMPi=(BMi)(Bpi)/(100-b). Among > 1000 patients, we identified those with CMi or CPi increased > normal 50-70%.

Results: Patients with high CMi and/or CPi had higher grade gliomas, meningiomas, cerebral aneurysms, postoperative craniopharyngioma, metastatic melanoma, and low values vs. normal ranges for BPi 95-125%, BMi 120-195%. BMPi is maximal near CMi 50%, and decreases for cortical indices either below or above normal. Regional activity indices multiplied by the ratio of 30% isocontour to regional isocontour area have correspondingly similar, normal ranges and are useful for focal abnormality analysis: eg. Abscess, ictal seizure loci, encephalomacia and focal neoplasia or hemorrhage.

Conclusion: Abnormal decrease in BMPi reliably predicts a broad spectrum of

pathophysiology arising either from abnormal increase or decrease CMi and/or CPi values.

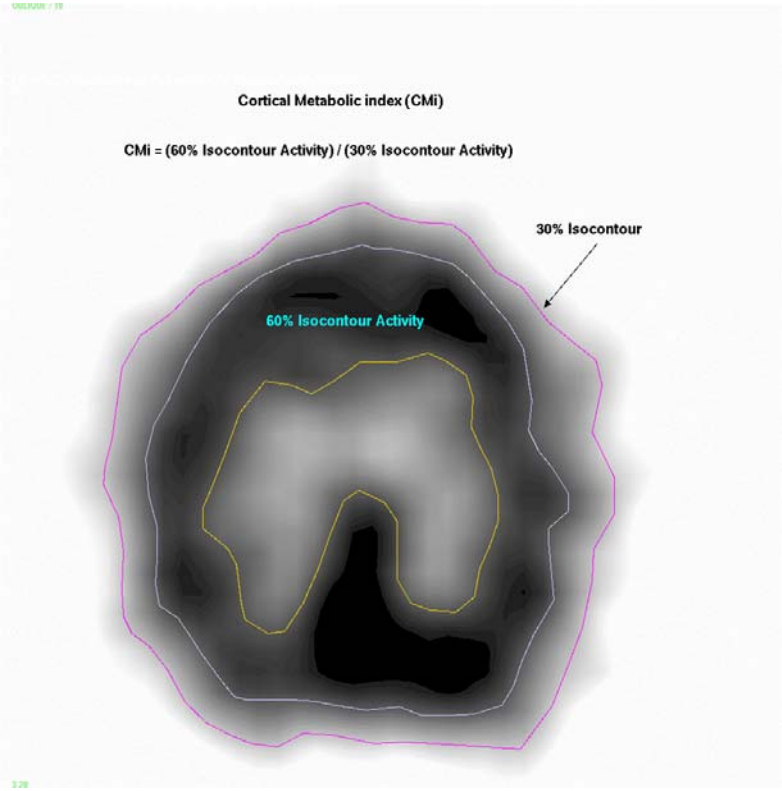
**1.** Cortical Metabolic indices were calculated from basal metabolic SPECT images using a metabolic tracer such as 200 MBq F-18 fluorodeoxy-glucose, 560 MBq Tc-99m-ECD or 500 MBq Tc-99m-HMPAO IV, given in a quiet dark room. The dual-head SPECT camera had 5.5 mm resolution using ultra-high resolution parallel-hole collimators, sensitivity 6500 cpm/MBq. Image matrix was 128 x 128 acquired in 64 frames/180 deg with 5 to 60 sec/frame (usually < 30 min per acquisition).

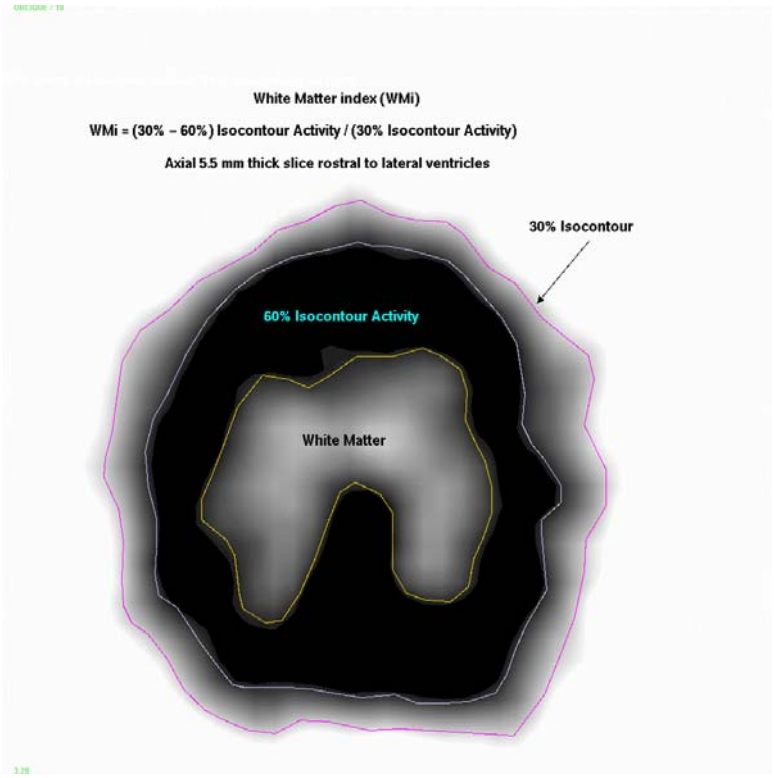
Cortical Perfusion indices were similarly calculated using perfusion stimulants such as 0.8 mg nitroglycerin sublingual, 0.5 to 1.0 g acetazolamide IV, 10 g omega-3 unsaturated fish oil oral or 100 mg cilostazol oral and IV perfusion tracers such as Tc-99m-HMPAO or Tc-99m-ECD at suitable time intervals thereafter.

Brain Metabolic indices were defined as: BMi = (CMi)(WMi) / b, where b is cerebral ventricular activity as a % of peak brain activity, typically near 20%, normalized by multiplying 20% by (20% / measured b), so that smaller measured b, corrected for scattering, (larger ventricles or more cerebral atrophy) leads to smaller BMi. Brain Perfusion indices were similarly calculated from perfusion-stimulated SPECT.

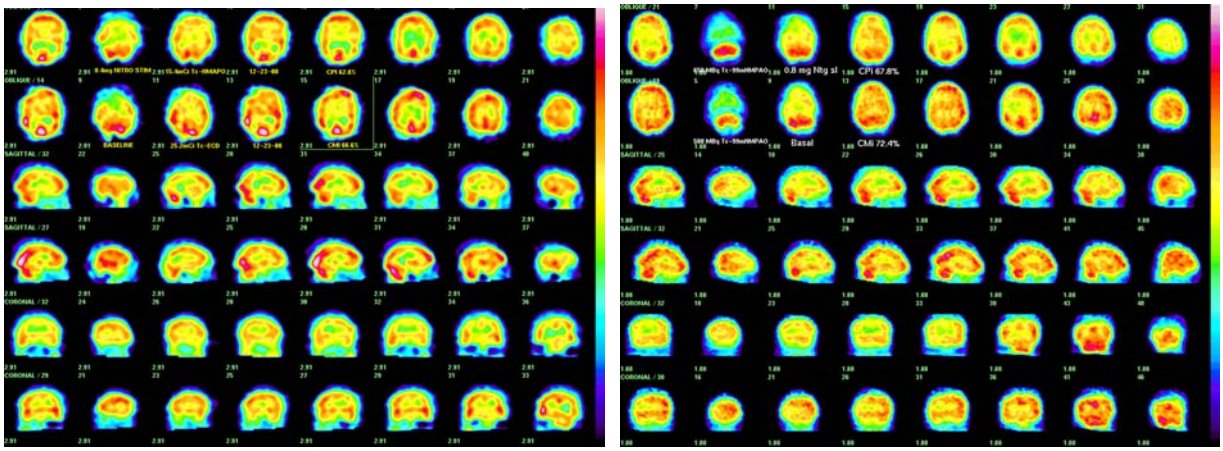
The Brain Metabolic-Perfusion index BMPi was a cross product of its components, BMi and BPi, scaled by dividing by the normalizing factor (1-b), for which b was taken as the simple average of the normalized b values calculated as described above for the perfusion study and that calculated for the metabolic study. Again, larger ventricles (with lower b and greater cerebral atrophy) decrease BMPi, indicating a decreased potential for recovery.

**2.**


Cortical Metabolic index (CMi)
CMi = (60% Isocontour Activity) / (30% Isocontour Activity)
30% Isocontour
60% Isocontour Activity


White Matter index (WMi)
WMi = (30% – 60%) Isocontour Activity / (30% Isocontour Activity)
Axial 5.5 mm thick slice rostral to lateral ventricles
30% Isocontour
60% Isocontour Activity
White Matter

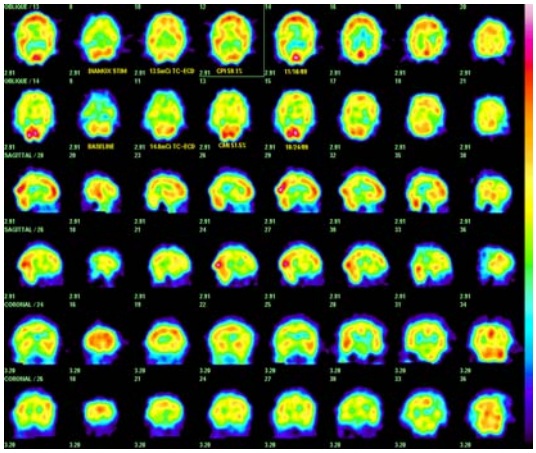
**3.** Brain SPECT below on the left, perfusion-stimulated on top and basal on bottom of 3 paired image rows, for a 53 y.o. sickle SC anemic woman who smokes > 1 pack/day cigarettes, has history of hyperlipidemia, hyperhomocysteinemia, hypertension and mild renal insufficiency (stage 2, GFR 65 ml/min) post right nephrectomy for obstructive uropathy, with CMi 66.6%, CPi 62.8%, BMPi 359%, whose anemia worsens in 6 months from hgb 11.1 to hgb 7.7 g/dl and develops, below on right, brain SPECT (same display format) with high CMi 72.4%, CPi 67.8% (note similarly compromised flow reserve), BMPi 475%, consistent with significant risk of an adverse event, as was development of frank jaundice with total bilirubin 4.7 g/dl, (direct 0.6 g/dl and indirect 4.1 g/dl) and high ferritin 624 ng/ml (normal <232 ng/ml).

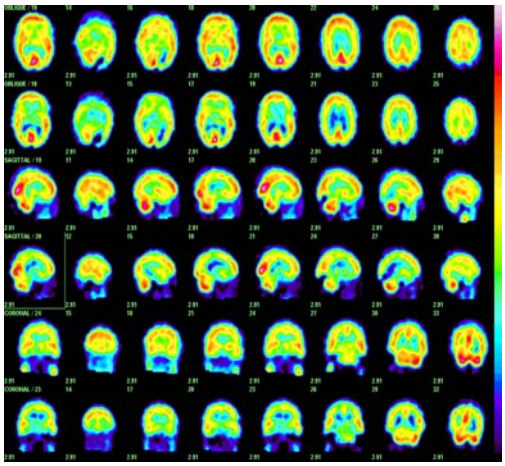


**4.** Follow-up Brain SPECT (similar format) for the same, now 54 y.o. sickle SC patient described above who, despite correction of her anemia to hgb 10.1 g and resolution of her jaundice, has developed glucose intolerance (random blood sugar 149 mg/dl or 8.41 mMol) and a minor stroke, shown as the green wedge-shaped peripheral left parietal defect in the axial basal images (second row). Misery perfusion is likely (subacute stroke) as the defect resolves in the stimulated images. Not unexpectedly, CMi 51.5% and CPi 59.1%, BMPi 307% are still supranormal, but suggest an improved prognosis, as also expected from her overall improved laboratory parameters.

Comparison brain SPECT with CMi 49.1%, CPi 53.6%, BMPi 200%, for a 60 y.o. hyperlipidemic, chronic thyroiditis, osteoporotic, menopausal, cardiac patient who developed a hemorrhagic stroke (MRI confirmed) 9 months prior to the SPECT scan,

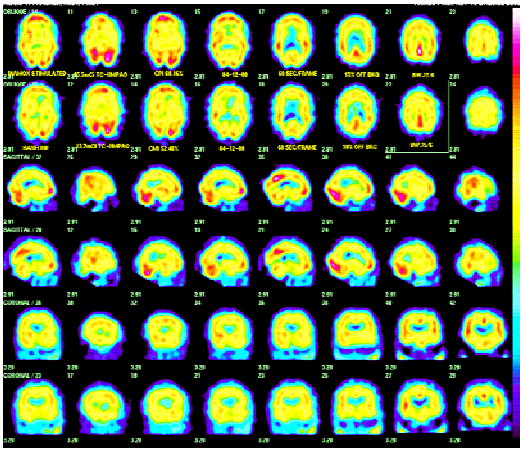
while being treated for prevention of percutaneous coronary angioplasty restenosis with aspirin 81 mg oral daily and clopidogrel 75 mg oral daily, the left occipital stroke which caused the expected homonymous hemianopsia.

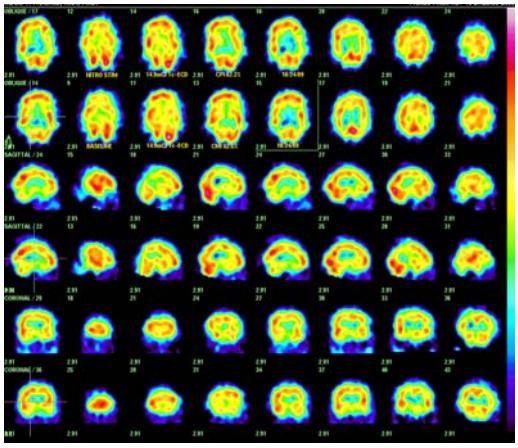




**5.** Brain SPECT, CMi 52.5%; CPi 60.2%, below on the left with perfusion-stimulated on the top and basal on the bottom, each of 3 paired rows of images, for a 73 y.o. man one month post emergency hypophysectomy for pituitary macro-adenoma (initially considered a craniopharyngioma from MRI imaging) which caused pituitary apoplexy, compromised the optic chiasm causing bitemporal visual field loss and more marked left eye vision loss, hypogonadism and eventually panhypopituitrism and complaint of memory loss, demonstrating residual tumor vs. postoperative change (focal, nodular increased tracer distribution) in saggital section 35 (third row, near center).

Follow-up brain SPECT, CMi 62.6%, CPi 62.2% (same image format) after 18 months, the patient having refused radiotherapy for possible residual tumor, reveals that the patient's diagnosis was more accurate than his physician's, the focal region of hyperfusion having completely resolved and the patient having developed no new symptoms nor compromise of his cortical indices, consistent with the initial finding representing postoperative change. Further experience is needed to apply the BMPi method for focal hyper-perfusion and/or hypermetabolic abnormalities which not infrequently are critical for accurate prognosis.





**Summary**

Abnormal increase in calculated indices of cerebral cortical metabolism and stimulated perfusion represent a broad spectrum of pathophysiologies including acute exacerbation of systemic illness, such as sickle SC anemia, focal benign or malignant neoplasia, cerebrovascular malformations, abscess or other neurotropic infection (particularly Herpes encephalopathy) or postoperative or other inflammation. Correlative studies of proven pathologic cases with initial and serial follow-up provide a framework for the development of useful quantitative indices of brain metabolism and stimulated perfusion which may aid in accurate diagnosis and in directing appropriate therapy dependant on accurate prognosis.