PseudoAlzheimer's Pattern of Brain Metabolism in Thyroid Disease and Mercury Toxicity Studied by Metabolic Stress Brain SPECT

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Abstract

Objective: Compare metabolic stress and basal brain SPECT results in thyroid and mercury-exposed patients.

Methodology: Brain SPECT used calculated metabolic and perfusion indices, Tc-99m-ECD IV, anticholinergic stress with 4 scopolamine patches > 4 hrs, Tc-99m-HMPAO IV, 1 g IV acetazolamide or similarly effective perfusion stimulant, the labeled tracers given in a quiet, dark room. Quantitative urine porphyrins monitored mercury exposure.

Results: Basal metabolic and perfusion-stimulated brain SPECT in 18 mildly hyper- and 24 midly hypothyroid patients with cognitive complaints typically revealed a pseudoAlzheimer's pattern of parieto-occipital and mesial temporal hypometabolism and/or hypoperfusion. Metabolic stress brain SPECT was well tolerated in 2 hyper- and 2 hypothyroid patients but did not show the pseudoAlzheimer's pattern. Psychiatric disease, thyroid autoimmunity and cognitive dysfunction, including an abnormal MiniMental Status Exam, coexisted in most patients. Two thyroid patients symptoms and brain SPECT normalized with 1 yr of 4 g/day omega 3 fish oil. Among 15 mercury toxic patients, many with pseudoAlzheimer's brain SPECT, mercury levels improved in 2 along with cognitive and fine motor symptoms, after ceasing mercury exposure or chelation therapy, and brain SPECT improved in one.

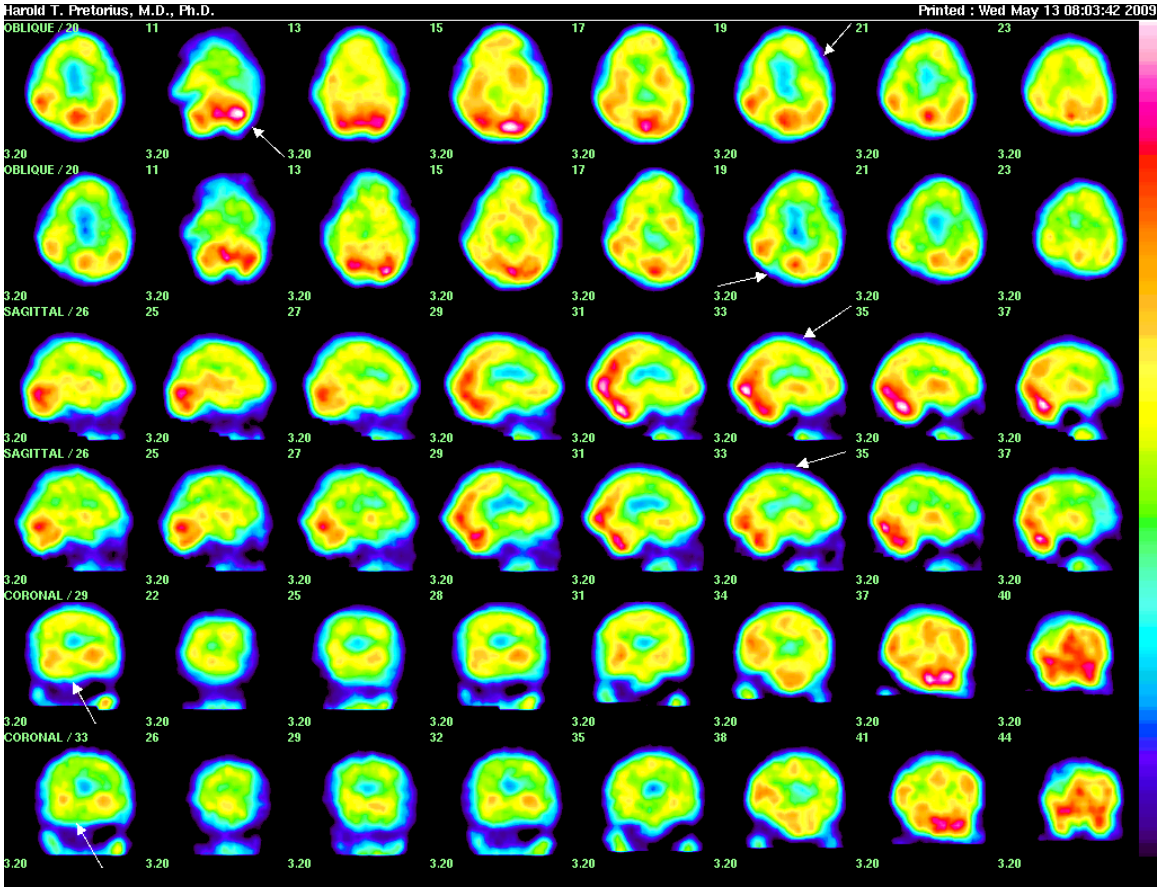
Discussion: Mild hyperthyroidism markedly increases incidence of Alzheimer's disease in prospective studies. Cogenital hypothyroidism due to Down's syndrome also results in cerebral pathology similar to Alzheimer's disease. Brain SPECT both in mild hyper- and mild hypothyroidism has a pseudoAlzheimer's pattern, similar to Alzheimer's disease except less severe. Whether Alzheimer's fundamental pathophysiology derives from metabolic defects in cerebral glucose metabolism, often called type 3 diabetes mellitus, or cerebral hypoperfusion contributing to abnormal amyloid and/or acetylcholine metabolism, is unknown. This study's data does not indicate a primary role for disruption of cholinergic neurotransmission, but supports primary glycolytic and resultant oxidative metabolic abnormality, since perfusion reserve, shown here and in earlier studies with multiple perfusion stimulants, is usually intact in early Alzheimer's or in thyroid patients, and since mercury induced oxidative injury clearly causes cognitive impairment and, when severe, dementia similar to Alzheimer's.

Conclusion: Association of thyroid and Alzheimer's diseases is a window of opportunity for novel neuroendocrine study such as metabolic stress brain SPECT. Our results emphasize key roles of glycolytic metabolism in autoimmune thyroid disease and oxidative injury in mercury toxicity.

1

A 59 year-old woman with probable hypophysitis, secondary hypothyroidism and multiple dental amalgams had hot flashes, low libido, memory loss and weight gain, unrelieved by internet-acquired Hoodia. A non-endocrinologist implanted testosterone (T) and estradiol (E2) pellets, raising her serum T to 176 ng/dl total, 3.1 ng/dl free T, and E2 to 78 pg/ml. Menopausal symptoms improved except for her memory, consistent with low CMi 41% and CPi 42.3% on brain SPECT, shown on the right, with basal metabolic images on the bottom and stimulated perfusion images on the top of the 3 paired image rows. This patient's urine corproporphyrin 1 of 36 mcg/L was high and her position well below the regression line (see panel 2) on the plot of CPi vs.urine corproporphyrin 1 levels: in vivo evidence that testosterone (or trace amounts of other neurotoxic metals) exacerbates mercury neurotoxicity, a phenomenon well established in vitro by Professorr Boyd Haley of the University of Kentucky.

Note arrows showing partial pseudo-Alzheimer's pattern with unilateral (right) parieto-occipital and right mesial temporal decrease in basal metabolism, largely ameliorated by perfusion stimulus which was a double dose of sublingual nitroglycerin in this case. Crossed cerebellar diaschisis is also present and has been associated with.



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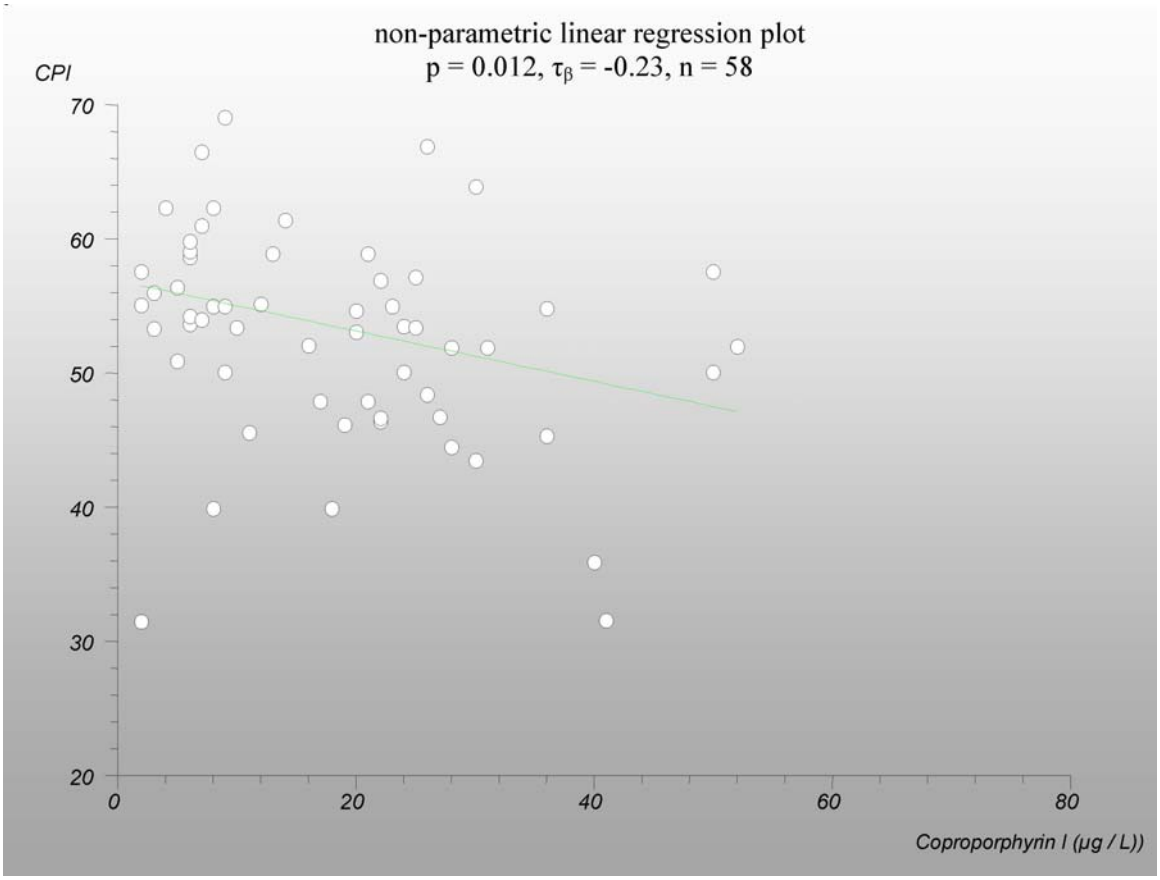

non-parametric linear regression plot
p = 0.012, τβ = -0.23, n = 58
CPI
70
60
50
40
30
20
0
20
40
60
80
Coproporphyrin I (µg / L))

3

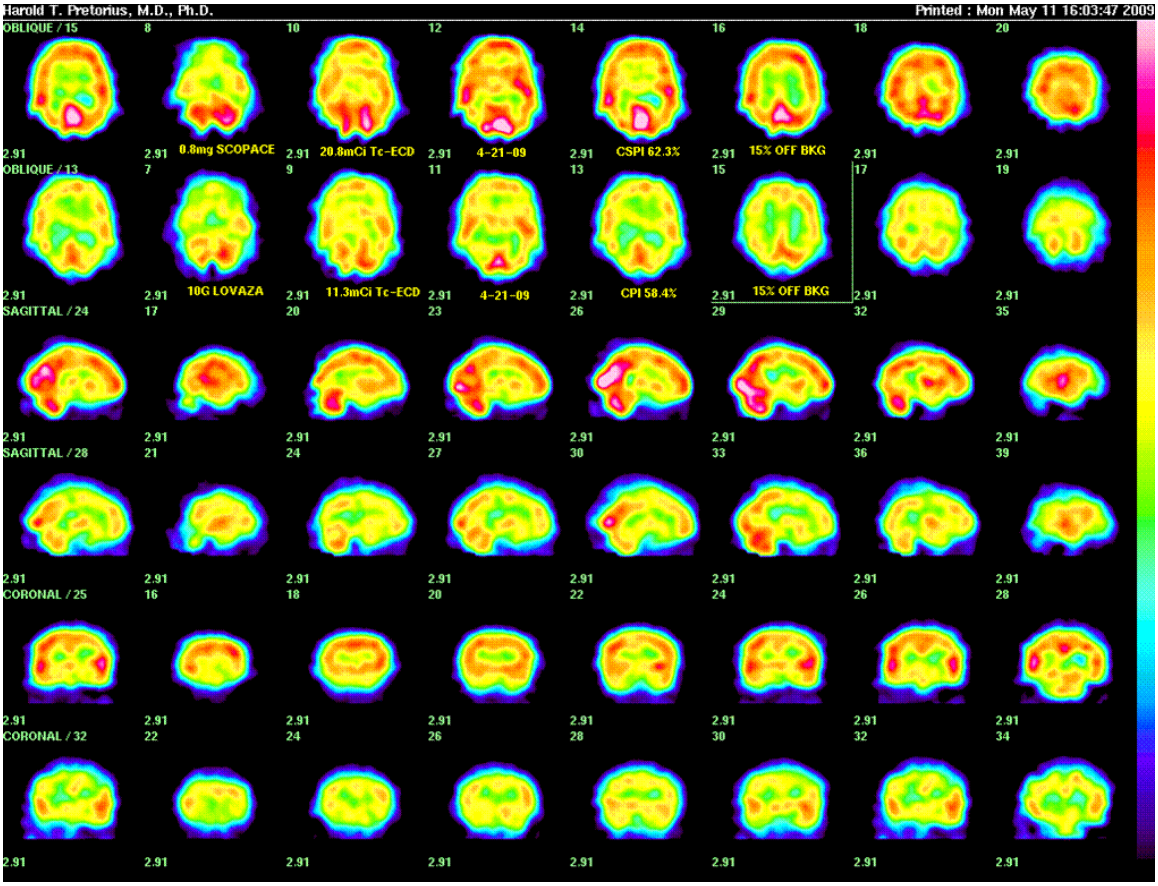
Descriptive Information	Overall (n = 58)
Gender	
Female / Male (ratio)	35 / 23 (1.4 : 1)
Age	
Mean Age in Years ± Std	51.9 ± 14.4
(range)	(23 – 80)
CPI (%)	
Mean ± Std	53 ± 7.8
(range)	(32 – 69)
Urinary Coproporphyrin I (µg / L)	[reference range = 0 – 15]
Mean ± Std	18.2 ± 13.0
(range)	(2 – 52)
Patient Diagnoses (%)[1]	
Diabetes	17 (29%)
Dementia/Memory Loss	18 (31%)
Fibromyalgia	6 (10%)
Bipolar/Depression	7 (12%)
Autoimmunity	10 (17%)

note: patients having received detoxification therapy, having Sickle Cell Anemia, or were a welder were excluded from the study sample.
[1] patients examined in the present study may have had one or more diagnoses.

4

A 50 year-old woman had concern about her risk of Alzheimer's disease which her mother, at age 68 years, her father, at age 58 years, and at least one paternal uncle in his 5th decade all developed, especially since her baseline brain SPECT (lower of each paired set of 3 rows of SPECT images opposite) was consistent with early neurodegeneration, a finding which may preceed development of typical clinical symptoms by at least several years.

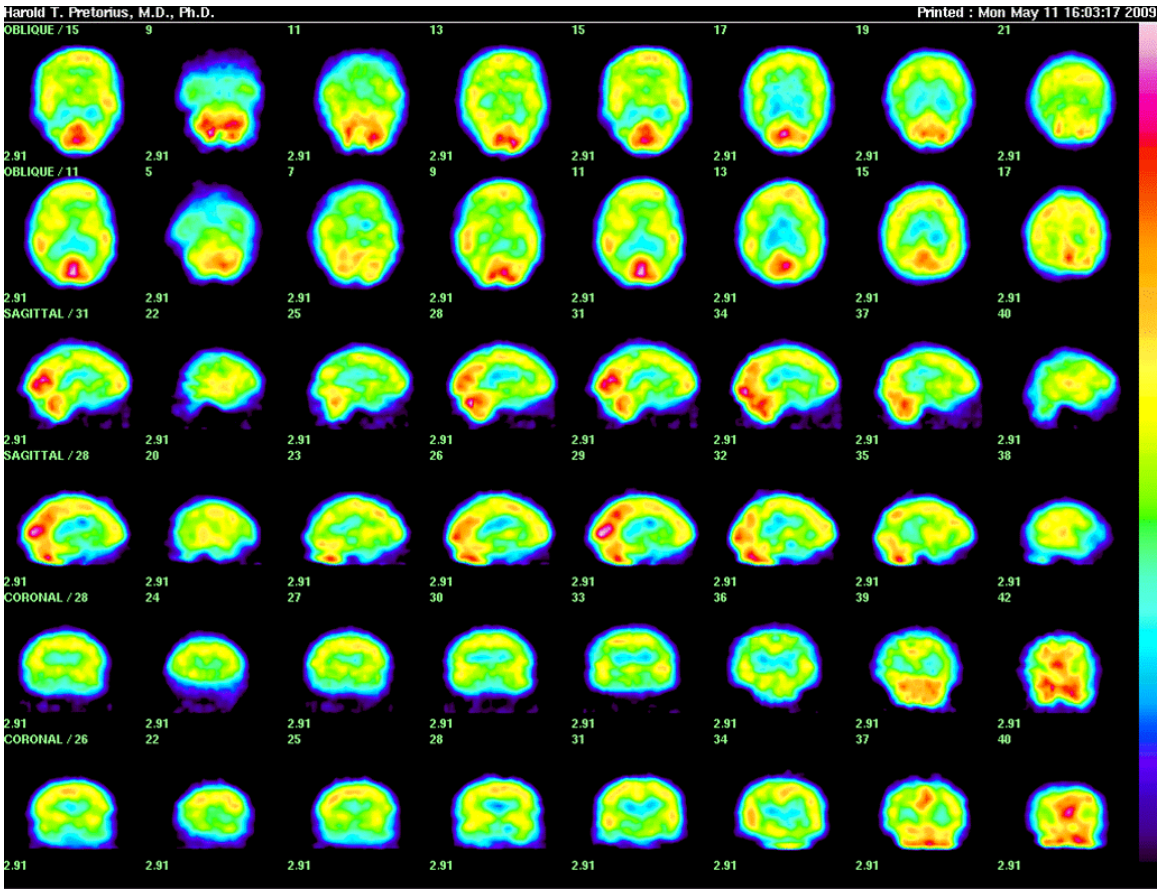
Not all studies are positive! Ms. Brotherton's metabolic stress brain SPECT (top of each of the 3 rows of paired images opposite) is clearly normal. In our experience, Brain SPECT is at least as predictive as cardiac SPECT; a negative study indicating that not only is Alzheimer's very unlikely to be present but furthermore that it will be very unlikely (probably less than 1% chance) to develop Alzheimer's for 3 to 5 years.



5

A 69 year-old hypertensive, American volunteer of the Hurricane Katrina among Tother disaster relief efforts complained of memory loss. Metabolic stress brain SPECT used 0.8 mg scopolamine oral and is shown in the top of each set of three paired rows to the right. Bilateral parieto-occipital and temporal abnormalities in the basal study (bottom of each of 3 paired rows of images) are consistent with neurodegeneration and mild cognitive impairment. The metabolic stress study shows enhanced abnormalities, especially posterior parietal (cf axial section 19 stimulated and 37 unstimulated, demonstrating its increased sensitivity to detect deficits in acetylcholine dependent neuronal networks.

The multifactorial role of pathophysiology typically contributing to cognitive impairment is emphasized by this patient's past history, which included labile hypertension due to pheochromocytoma, which was successfully removed with improvement in hypertension control but may well have contributed to periventricular or other deficits in neuronal perfusion and metabolism.



6

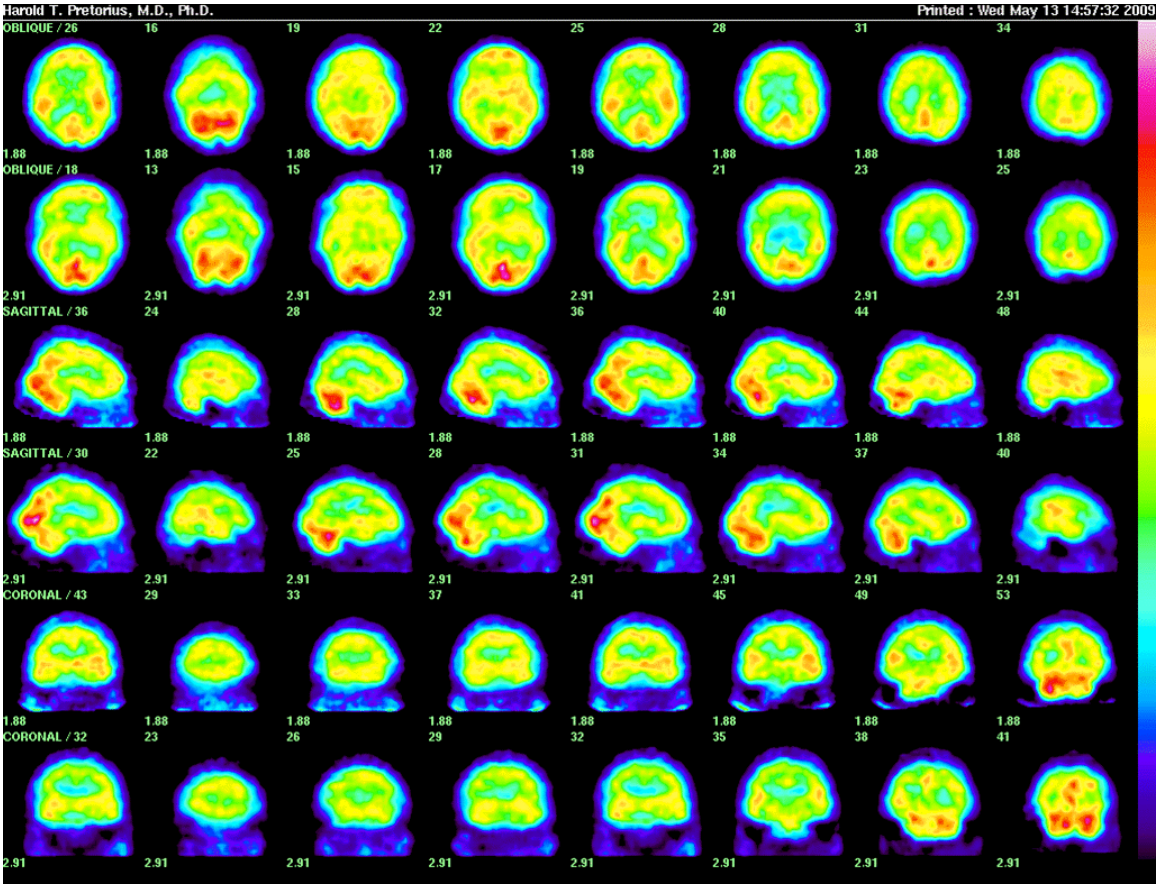
A 60 year-old insulin-dependent type 2 diabetic patient recovered spontaneously from thyroiditis and is euthyroid with TSH 1.90, T3 142 and Free T4 1.4, all normal prior to the Dual Camera Emmission Computed Tomography (DCECT) shown below. Advantages of this method include:

Similar study statistics and true resolution, the first one obtained on a dual head SPECT and the second on a single head SPECT since same day second studies have nearly twice the activity of the first.

Preventing claustrophobia by scanning behind the patient over 180 degrees, left lateral to right lateral.

Dual isotope and dual camera (DICECT) function, further increasing efficiency.

Findings in this patient are believed due to small vessel cerebrovascular disease and nonspecific neurodegeneration, a common pattern overlapping with the pseudoAlzheimer's pattern in both thyroid and diabetic patients which may not necessarily specific to either one. This patient also had small vessel coronary disease documented by coronary angiography, a pattern postulated more typical of women; however, this patient is a man. His MMSE was 27, showing the sensitivity of the present method.



Conclusion

1. Patients with thyroid disease and memory complaints frequently show nonspecific neurodegenerative abnormalities on brain SPECT. These are less severe than actual Alzheimer's disease; however, not infrequently involve similar areas of the brain and hence may be termed pseudoAlzheimer's.

2. An unexpectedly high number, about 20% of patients with memory loss and autoimmune thyroid disease or other autonomous thyroid function have abnormal fractionated urine porphyrins, consistent with metal toxicity, likely mercury with or without trace levels of other metals, which typically produces abnormalities in coproporphyrin I and III.

3. Even a mildly supraphysiologic level of total and/or free testosterone is likely to potentiate and exacerbate neurotoxicity associated with a low-level body burden of mercury.

4. The DICECT (Dual Isotope/Camera Emission Computed Tomography) method provides a convenient and sensitive measure of brain function in neuroendocrine patients and offers potential for further diagnostic and therapeutic study.