positive symptoms decreased; remaining negative symptoms correlate negatively to rCBF in different locations. Especially for difficulties in abstract thinking, an exclusive lateralization to the right side is found, which shows that both hemispheres are involved whenever negative symptoms predominate. These findings may explain inconsistent recent results in rCBF patterns in drug-naive or neuroleptic-treated schizophrenic patients.

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Asymmetry of Basal Ganglia Perfusion in Tourette's Syndrome Shown by Technetium-99m-HMPAO SPECT

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Our study involved performing brain perfusion SPECT scans on Tourette's subjects to observe any common perfusion abnormalities involving the cerebral cortex or subcortical structures. **Method:** Six patients with Tourette's syndrome and nine normal control subjects underwent a brain SPECT study with ^{99m}Tc-HMPAO. Regions of interest were generated over the cerebral cortex, basal ganglia, thalamus and cerebellum to evaluate any relative perfusion abnormalities or asymmetry in the Tourette's subjects. **Results:** Five of the six Tourette's subjects demonstrated a significant decrease in right basal ganglia activity which was not present in any of the normal control subjects. **Conclusion:** Our study suggests an etiology for Tourette's syndrome involving the right basal ganglia. Furthermore, brain SPECT may be useful in the evaluation of these patients if it proves to be sufficiently sensitive and specific in larger study populations.

Key Words: Tourette's syndrome; SPECT; basal ganglia

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Gilles de la Tourette's syndrome is a common neurologic disorder characterized by chronic multiple motor and vocal tics. It may occur by itself or in association with an obsessive-compulsive disorder in approximately 55% to 74% of cases (*1*). Although the precise etiology of this disorder is unknown, several observations suggest a dysfunction of the dopaminergic systems in the basal ganglia or cortico-striatal thalamic pathways (*2*). These include an observed worsening of tics with catecholamine-stimulating drugs such as stimulants and a decrease of symptoms with dopamine antagonist medications. There is also an association of Tourette-like symptoms with several basal ganglia disorders such as tardive dyskinesia, postencephalitic parkinsonism and carbon monoxide encephalopathy (*3*).

This preliminary study was performed to observe any detectable perfusion abnormalities involving the basal ganglia or other subcortical structures in Tourette's subjects to further our understanding of this disorder.

MATERIALS AND METHODS

Six right-handed, drug-naive subjects who met DSM-III criteria for Tourette's syndrome were studied by SPECT. The study group included three women and three men ranging in age from 26 to 54 yr with a mean age of 36 yr. All Tourette subjects were recently diagnosed and recruited from the University of Rochester Medical Center outpatient neurology clinic. All had a negative history of any current or previous neuroleptic medication at the time of their SPECT study. The nine normal control subjects included five women and four men ranging in age from 56 to 81 yr with a mean age of 70 yr. All control subjects were in excellent general health and free of any history of neurologic or psychiatric illness, head trauma or surgery, or use of psychotropic or neuroleptic medication. The Tourette's group and normal control subjects were imaged using the identical SPECT protocol.

All SPECT studies were performed with a Trionix Triad triple-head gamma camera with a standard SPARC-10 workstation using ultra-high resolution collimators. All subjects were injected with 20 mCi (740 mBq) ^{99m}Tc-HMPAO with eyes open in a quiet, dimly lit room, with acquisition starting 20 min after injection. The subjects were imaged on a SPECT table with the head in a foam headrest with a velcro strap to minimize motion. The patients' cantho-meatal line was positioned perpendicular to the camera heads. The imaging protocol used a circular orbit in step-and-shoot mode with 30 projections (4° sample interval) of 40 sec per projection. Image data were acquired in 64 × 64 mode with a 1.2 mag setting. Data reconstruction was performed by filtered backprojection using a Hamming filter. The reconstructed study comprised approximately 5 million counts. Each image slice was 2 pixels (7.4 mm) in thickness.

Relative activity for various regions of the brain was derived by visually selecting a transverse slice through the midcerebral cortex that best demonstrated the basal ganglia and thalamic structures. Regions of interest (ROIs) were generated manually over the right cerebral hemisphere in the frontal, temporal and parietal regions as well as the right basal ganglia and thalamus. These regions were then flipped over without changing their size or shape to create identical mirror-image ROIs for evaluating the corresponding anatomic structures in the contralateral cerebral hemisphere (Fig. 1). A separate transverse slice through the midcerebellum was used for evaluating cerebellar activity. All regional activity was expressed as a ratio of counts per pixel relative to average cerebellar activity. This method was used for regional brain analysis of all study and control subjects.

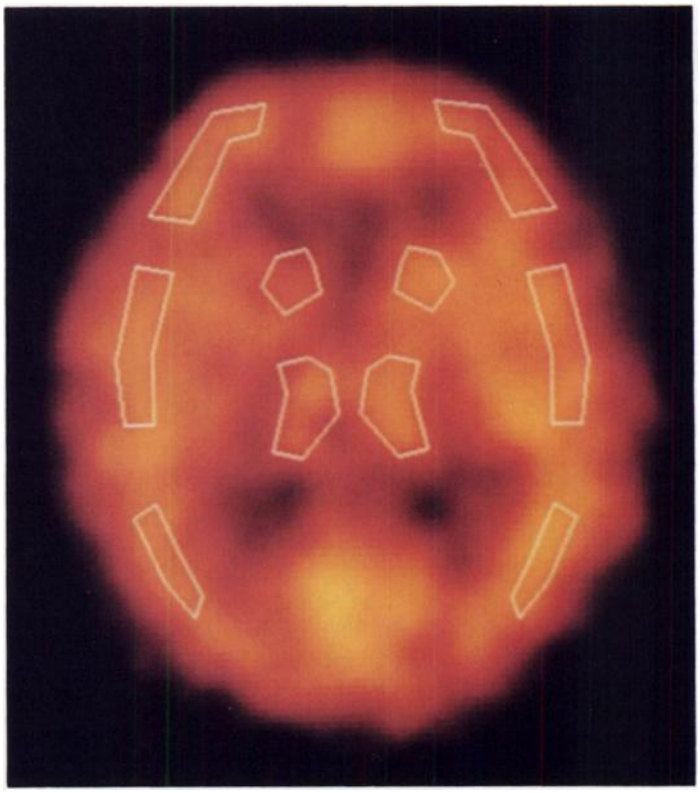

FIGURE 1. Transaxial brain slices illustrating ROIs for cerebral cortex, basal ganglia and thalamus.

RESULTS

The most significant finding in the Tourette's subjects was an asymmetry of the basal ganglia with relative hypoperfusion on the right side in all six patients (Fig. 2). This finding was not seen in the control subjects who consistently showed symmetric basal ganglia activity (Table 1). When a basal ganglia-to-

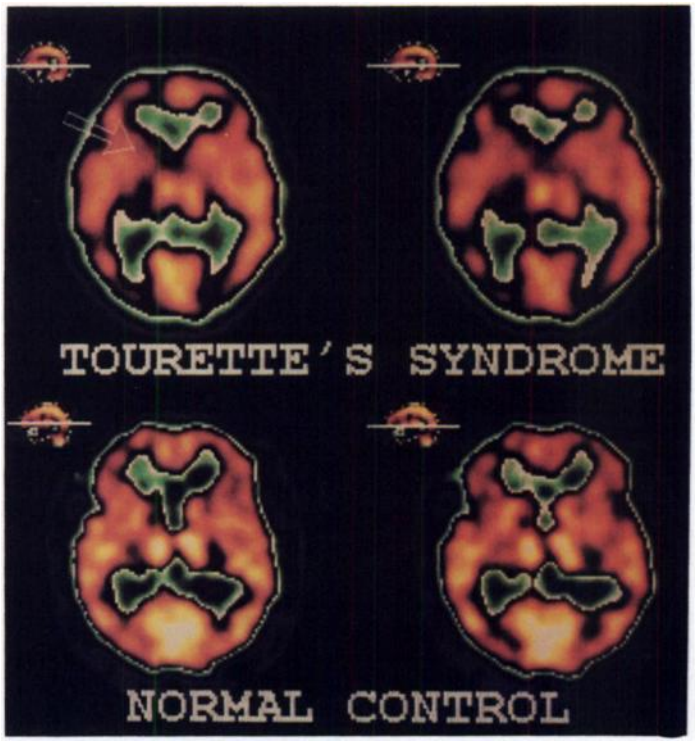

FIGURE 2. (A)Transaxial brain slices through the basal ganglia demonstrate reduced activity on the right side depicted by arrow. (B) Transaxial brain slices of a normal control patient show symmetry of the cortex and subcortical structures.

TABLE 1
Basal Ganglia Asymmetry (Right/Left Ratio)

Normal control subjects (n = 9)	Tourette's subjects (n = 6)
0.94	0.97
0.96	0.85
1.03	0.90
1.01	0.82
1.01	0.88
1.05	0.82
1.08	
0.95	
1.00	

Mean = 1.003 (s.d. = 0.047) for control subjects; mean = 0.883 (s.d. = 0.051) for Tourette's subjects; $p < 0.001$ is the statistical significance between both groups.

cerebellum activity ratio was calculated for each cerebral hemisphere, there was no difference between the Tourette's subjects and the control group on the left side, while the right basal ganglia-to-cerebellum ratio was reduced in the Tourette's group (Table 2).

The frontal cortex-to-cerebellum ratio was also compared between the Tourette's group and the control group. The Tourette's group demonstrated a mild relative hypoperfusion in the midfrontal cortex which was not statistically significant (0.722 ± 0.14 versus 0.787 ± 0.10). There was no significant asymmetry in the frontal, temporal or parietal cortex observed in either group.

An unpaired Student's t-test confirmed that the asymmetry of the basal ganglia in the Tourette's group was statistically significant ($p < 0.001$). Use of the basal ganglia-to-cerebellum ratios for each side revealed that the reduced uptake values on the right side were not sufficient enough to be statistically verifiable ($p = 0.11$). In all probability, this was because of the wide range in basal ganglia-to-cerebellum activity ratios observed within the control group (0.67–1.04 on the right; 0.65–1.10 on the left) as well as the small size of the study group. Use of the basal ganglia right-to-left ratio provided a much narrower variability range within the control group.

DISCUSSION

A review of the related literature shows marked inconsistency in SPECT and PET imaging findings in Tourette's subjects. Chase et al. (*4*) described decreased [^{18}F]FDG metabolism in the frontal, cingulate and inferior corpus striatum in 12 untreated Tourette's subjects using a high-resolution PET scanner. They further observed that the degree of hypometabolism in these regions correlated directly with the clinical severity of the patients' vocal and motor tics. Their findings suggest a neuronal hypofunction in certain striatal areas of the limbic system.

TABLE 2
Basal Ganglia Activity in Tourette's and Control Groups

	Control (n = 9)	Tourette's (n = 6)	
BG R/L Ratio	1.003 (s.d. = 0.047)	0.883 (s.d. = 0.051)	$p < .001$
Rt. BG/CBLM	0.87 (s.d. = 0.12)	0.76 (s.d. = 0.15)	$p = .11$
Lt. BG/CBLM	0.87 (s.d. = 0.13)	0.86 (s.d. = 0.12)	$p = .89$

BG = basal ganglia; CBLM = cerebellum

Riddle et al. (*5*) also described a study of nine drug-free Tourette's subjects demonstrating decreased activity in the left putamen-globus pallidus using ^{99m}Tc-HMPAO SPECT. A similar finding was described by Sieg et al. (*6*) in a case report of an 11-yr-old girl with Tourette's syndrome whose ^{99m}Tc-HMPAO SPECT study demonstrated markedly decreased activity in the left basal ganglia with a normal T-2 weighted MRI exam. It is unclear why these studies showed decreased basal ganglia activity on the left side, while our study showed only right-sided abnormalities. It is also uncertain whether these basal ganglia abnormalities are solely the result of the Tourette's syndrome or if obsessive-compulsive symptoms often associated with Tourette's syndrome contribute to these observed abnormalities. This question is raised by a case report by Hamlin et al. (*7*) of a 17-yr-old boy with obsessive-compulsive disorder and no Tourette's syndrome, who demonstrated decreased activity in the right basal ganglia on an [^{123}I]IMP brain SPECT study. This abnormality later normalized after clinical improvement with fluoxetine and amoxapine therapy, suggesting basal ganglia involvement in pure obsessive-compulsive disorder. Despite the inconsistencies in anatomic localizations for observed disturbances in physiologic imaging in Tourette's syndrome patients, recent studies have been in agreement in identifying relative differences between the left and right sides of the brain.

Two recent studies using MRI also concluded that there is an alteration in the comparative left compared with right relationship of basal ganglia volumes in patients with Tourette's syndrome (*8,9*). In particular, Tourette's syndrome patients demonstrated a relative reduction in left-sided volumes. It remains unclear how these anatomic findings relate to our own physiologic observations of reduced right basal ganglia perfusion. It has been hypothesized that the basal ganglia abnormalities observed in Tourette's syndrome are the result of a deficiency involving the dopaminergic or serotonergic pathways which innervate the basal ganglia (*10*). However, several studies fail to support the dopaminergic etiology for Tourette's syndrome. This includes a study by Turjanski et al. (*11*) using the postsynaptic D2 receptor binding agent ^{11}C-raclopride and PET, which showed no difference in D2 postsynaptic receptor density between five untreated Tourette's patients and a normal control group. They also observed no difference in striatal presynaptic dopaminergic activity between Tourette's subjects and normal controls using ^{18}F-DOPA and PET. Furthermore, they found no significant difference between neuroleptic-treated and untreated Tourette's subjects with either PET tracer. A similar study by Singer et al. (*12*) used ^{11}C-N-methylspiperone to label postsynaptic D2 receptors in the striatum and also found no difference in D2 receptor function between 19 Tourette's subjects and a normal control group.

Taken together, recent physiologic and anatomical imaging studies in Tourette's subjects have consistently identified an altered relationship between the left and right basal ganglia. Our preliminary study points to a relative reduction in perfusion to the right basal ganglia in Tourette's subjects although a larger study group would be necessary to statistically confirm this finding. Further studies are needed to better characterize the pathophysiologic mechanisms in this condition.

CONCLUSION

Our study showed a significant asymmetry of basal ganglia activity with a relative decrease on the right side in five of six Tourette's subjects, which was not present in any of the normal healthy control subjects. These findings are in keeping with a number of recent physiologic and anatomical imaging studies in

Tourette's syndrome that have identified altered relationships between the basal ganglia on the two sides. The nature of this relationship needs to be clarified. Additional studies to evaluate other mechanisms, such as serotonin receptor function, are required to better define the pathophysiology of this disorder.

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PET with L-[1-Carbon-11]-Tyrosine to Visualize Tumors and Measure Protein Synthesis Rates

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We studied the potential of PET with L-[1-^{11}C]-tyrosine (TYR) to visualize tumors outside the central nervous system and to quantify their protein synthesis rates (PSRs). **Methods:** Twenty-two patients suspected of having a malignant tumor underwent a PET study with TYR before biopsy. The PSR in nanomoles per milliliter tumor tissue per minute as well as the PSR in contralateral normal tissue, standardized uptake values (SUVs) and tumor-to-nontumor-ratios (T/N ratios) were calculated. **Results:** Fifteen of the 16 malignancies (94%) were correctly visualized as a hot spot. A chondrosarcoma of the sacrum was not visualized. Of the six patients with benign lesions, cold spots were correctly identified in four (67%). A benign schwannoma and an intramuscular hemangioma of the forearm were visualized as hot spots. PSR in tumor tissue was higher than in the corresponding contralateral normal tissues. PSR and SUV in malignant tumors were higher than in benign tumors. **Conclusion:** TYR appears to be a good tracer for imaging malignancies. The PSR, which was higher in malignant tumors than in normal tissue and the studied benign lesions, could be quantified and correlated with the SUV.

Key Words: PET; carbon-11-tyrosine; protein synthesis rate

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The potential of PET to diagnose cancer and monitor therapeutic response is widely recognized. Whereas advanced imaging techniques such as CT and MRI are based on the imaging of anatomy, PET enables the visualization of metabolism and (patho)physiology. This complementary information may be advantageous, e.g., detection of metastases (*1–3*). The main disadvantages of PET, i.e., its complexity and high cost, are at this stage outweighed by its higher resolution and greater sensitivity compared to SPECT (*4*). Even with the possibility of performing coincidence measurements with positron emitters in SPECT cameras, the major advantage of PET remains the ability to quantify metabolism, which makes it a powerful tool for grading malignancy and monitoring the effect of therapy (*5*).

So far, 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG) has been the most widely used radiopharmaceutical, based on the fact that tumor cells have increased glucose uptake. However, the use of FDG has several disadvantages, such as high background uptake in normal brain tissue, low specificity and uptake in inflammatory tissues (*6,7*). Therefore, there is a need for alternatives. Ishiwata (*8*) has shown that the uptake of amino acids is also high in tumor tissue due to an increased protein synthesis rate (PSR). Amino acids play a minor role in the metabolism of inflammatory cells (mainly neutrophils) compared to FDG (*9,10*). The measurement of ^{11}C-labeled amino acid uptake may be a better way to predict tumor growth rate than the glucose consumption rate measured with FDG. The majority of PET studies seeking to establish its predictive value for grading malignancy (*11,12*) and assess the effect of surgery (*13*) and radiotherapy (*12*) have been performed with L-[methyl-^{11}C]-methionine (MET). MET reflects amino acid uptake rather than protein synthesis. Since MET is involved in other metabolic pathways, such as transmethylation and polyamine synthesis, and it is converted into S-adenosylmethionine, a methyl group donor, which may lead to the accumulation of a variety of nonprotein metabolites in tumor tissue (*14–16*). This complicated metabolism of methionine has made it impossible to create a precise metabolic model. Carboxyl-labeled amino acids, such as L-[1-^{11}C]-tyrosine (TYR) (*17*), L-[1-^{11}C]-methionine (*15*) and L-[1-^{11}C]-leucine (*18*), appear to be more appropriate compounds to determine protein synthesis in tumors, because the main metabolite of these amino acids is $^{11}CO_2$, which is rapidly cleared from tissue and exhaled. Therefore, $^{11}CO_2$ does not contribute substantially to the ^{11}C radioactivity in tumor tissue as measured by PET (*8,19*).

At our institute, a model has been developed to determine the

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