Brain SPECT in Sydenham's Chorea in Remission

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ABSTRACT

Background: Sydenham's chorea, a major manifestation of rheumatic fever, is characterized by chorea, behavioral changes, and cognitive dysfunction. Perfusion changes in the basal ganglia are the most frequent imaging findings observed in patients with Sydenham's chorea.

Methods: Twelve adult women with Sydenham's chorea in remission underwent brain single-photon emission computed tomography (SPECT). Their scans underwent a quantification process to evaluate the perfusion of Brodmann's areas of the frontal lobes and basal ganglia. The results were compared with the findings from a control group that was matched by age.

Results: A pattern of hyperperfusion in the left putamen was observed in the patient group ($P = 0.02$). No significant difference was observed in relation to other brain regions.

Conclusions: The findings of brain SPECT suggest that perfusion abnormalities of the basal ganglia may persist even after the remission of abnormal movements in patients with Sydenham's chorea. © 2013 International Parkinson and Movement Disorder Society

Key Words: Sydenham's chorea; SPECT; perfusion; basal ganglia; putamen

Sydenham's chorea (SC), one of the main criteria of rheumatic fever, is characterized by chorea and other abnormal movements as well as behavioral symptoms and deficits of executive function. All of these abnormalities have been explained by the disruption of the frontostriatal loops found in SC.[1]

Although structural neuroimaging in patients with SC rarelyr shows abnormalities, functional neuroimaging is more commonly associated with changes in brain perfusion and metabolism. Most patients present with hyperperfusion or hypermetabolism in the basal ganglia, whereas hypoperfusion is a less common finding.[2-13] In addition, hypoperfusion in the frontal lobes also has been described.[9,10] In contrast, approximately 20% of patients evaluated have not had an abnormality of brain perfusion.[3,6,8,10]

In most studies, perfusion abnormalities are present in the acute phase of the disease and tend to disappear at subsequent evaluations.[5,8] However, there is some evidence that at least a subset of SC patients may present with brain perfusion abnormalities even after the disappearance of abnormal movements.[9]

The usual method for evaluating changes in brain perfusion has been visual analysis. Rarely, a semiquantitative technique has been used to analyze the evaluations.[5,8] To improve the evaluation of brain perfusion in these patients, we used a quantitative method to examine the basal ganglia and frontal areas.

Patients and Methods

Twelve women who had SC in remission (defined as the absence of chorea without treatment) according modified Jones criteria underwent brain single-photon emission computed tomography (SPECT).[14] All patients were followed in our movement disorders unit and were evaluated using the Federal University of Minas Gerais Sydenham's chorea rating scale (USCRS).[15] The study was approved by the local ethics committee, and all participants signed a written consent form.

Patients were placed in a quiet, dimly lit room. Ethyl cysteinate dimer-^{99m}Tc was administered intravenously at the usual dose of 740 to 1.110 MBq. Brain SPECT images were obtained 60 minutes after the injection using a dual-head gamma camera equipped with low-energy, high-resolution, parallel-hole collimators (ADAC Vertex Plus Gamma Camera; Philips Healthcare, Andover, MA). We acquired 120 projections at 60 projections per head (30 seconds per projection) over 30 minutes using a matrix size of 128 × 128.

The data from each patient were exported into a DICOM format on a Mirage workstation (both from GE Healthcare, Little Chalfont, UK), and the

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quantification of cerebral perfusion was performed in NeuroGam software (Segami Corporation, Columbia, MD). The processing of the raw data was performed using a ramp filter, and reconstruction was performed using filtered back projection. A Chang attenuation correction of 0.12 cm^{-1} was applied, and the data were post-filtered using a Butterworth filter (order, 9; cutoff, 0.32 cycles per cm).

During the data acquisition process, the traditional images were adjusted to a Talairach map and underwent a step known as anatomic standardization. Next, we employed a functional normalization step in which the user could alter the results by choosing the reference point of the maximum neuronal activity.

A region-of-interest automated technique was used by the NeuroGam program to compare regional blood flow abnormalities in the brain. Images were mapped, and review displays were generated, including 3-dimensional perfusion visualizations of the cortex, basal ganglia, and cross-sectional slices. Based on available Brodmann's areas, the program quantified activities in the brain volumes. Each hemisphere was subdivided into six rectangular volumes, which underwent a specific affine transformation to fit the Talairach atlas. This method allows quantitative and qualitative comparison of sequential brain images on the same patient as well as brain images on a given patient against a normal database.

The following areas were quantified in both hemispheres: caudate nucleus, putamen, thalamus; and Brodmann's areas 6, 8, 9, 10, 11, 24, 25, 32, 44, 45, 46, and 47. After the quantification process of specific brain areas, the results were compared with those from 18 sex-matched and age-matched controls. The control group was composed of healthy women ages 18 to 30 years who had no neurologic or psychiatric disorders.[16]

In addition, the perfusion abnormalities were correlated with SC variables, such as mean age at disease onset, mean disease duration, the number of episodes, the clinical pattern of chorea, and the presence of carditis. All patients were on prophylactic penicillin G benzathine.

Comparisons between the control group and the patient group were made using the Mann-Whitney test. Correlations between perfusion abnormalities and clinical variables of the disease were made using Spearman coefficients. P values < 0.05 were considered statistically significant. Statistical analyses were performed using the Statistical Package for Social Sciences for Windows (version 17.0; SPSS Inc., Chicago, IL).

Results

The mean age (± standard error) was 23.5 ± 4.3 years (median, 23 years) in the patient group and 25.3 ± 3.0 years (median, 26 years; range, 19-30 years) in the control group. There was no difference between groups in relation to age ($P = 0.15$). In the patient group, the mean age at disease onset was 15.6 ± 4.3 years, and the mean disease duration was 2.3 ± 2.2 years. In relation to the number of SC episodes, six patients presented with one episode, two patients presented with two episodes, and four patients presented with three episodes. All recurrences presumably were streptococcus-induced, and none were estrogen-induced. In relation to the form of the disease, eight patients presented with generalized chorea (66.7%), one patient presented with left hemichorea (8.3%), and three patients presented with right hemichorea (25%). Carditis was diagnosed in six patients (50%). The mean time between the remission of choreic movements and the brain SPECT was 5.5 years (range, 1-10 years).

TABLE 1. Perfusion comparison of the caudate nucleus, putamen, and thalamus of controls and patients

	Mean (standard deviation)		
Brain region	Controls	Patients	*P*
Left caudate nucleus	57.0 (5.3)	61.1 (6.1)	0.07
Right caudate nucleus	58.5 (5.1)	62.1 (8.1)	0.20
Left putamen	75.4 (5.1)	80.7 (6.0)	0.02
Right putamen	76.8 (6.2)	79.4 (7.3)	0.62
Left thalamus	69.8 (7.7)	71.2 (6.9)	0.70
Right thalamus	68.4 (9.0)	68.5 (6.7)	0.90

There was no significant difference in the perfusion of Brodmann's areas between controls and patients. The results from the quantification of perfusion in subcortical regions are presented for both groups in Table 1. Patients presented more often with hyperperfusion in the left putamen compared with controls ($P = 0.02$). Patients had higher perfusion values in the left caudate and in the right basal ganglia, although the difference from values in controls failed to reach statistical significance. Additional analysis indicated no significant correlation between hyperperfusion of the left putamen and clinical SC variables. In addition, using brain SPECT, we did not observe any correlation between the time to remission of SC and the perfusion of basal ganglia.

Discussion

Our study is the first to use a brain SPECT technique to quantify perfusion in patients with SC. We observed hyperperfusion in the left putamen more often in our patient group compared with our control group. The pattern of hyperperfusion in basal ganglia has been described previously in patients with SC.[3] However, the results from the current work contrast with previous results, which indicated the return of normal brain perfusion after the remission of abnormal movements. In those studies, the patients underwent the examination close to the time of diagnosis and, in some patients, a few months after the onset of the disease, which suggests a higher probability of finding changes in the initial phases.[5,8]

Although the caudate is normally associated with the appearance of chorea, lesions in other brain areas, including the putamen, also may be associated with chorea.[17] In our sample, three patients had right hemichorea, whereas only one patient had left hemichorea. This clinical finding may be correlated with the observed increase in the perfusion of the left basal ganglia in our patients.

We also observed the absence of abnormal perfusion in cortical frontal areas. In other studies, visual analysis of brain SPECT demonstrated a pattern of hypoperfusion in frontal areas.[9,10] Another finding of our work was the absence of a correlation between hyperperfusion of the left putamen and the clinical variables of SC, such as age at symptom onset, disease duration, the number of episodes, the pattern of chorea, and the presence of carditis. The reduced number of patients in our sample may have contributed to the lack of correlation between the neuroimaging findings and the clinical variables of SC. A pattern of unilateral hyperperfusion of the basal ganglia associated with contralateral hemichorea has been described in a reduced number of patients with SC in the acute phase of the disease.[3] The proposed mechanism to explain the changes in perfusion of the basal ganglia in SC is an alteration in the blood-brain barrier induced by inflammation in these regions.[6] The results from our study suggest that the inflammatory phenomena in basal ganglia in SC may be persistent. In other etiologies of chorea, such as Huntington's disease, neuroacantocitosis, and vascular chorea, a pattern of hypometabolism in the basal ganglia has been demonstrated.[18-22] However, in chorea associated with inflammatory disorders, such as systemic lupus erythematosus, limbic encephalitis, and antiphospholipid antibody syndrome, hyperperfusion or hypermetabolism may occur in the basal ganglia.[22-25] Although we failed to identify any correlation between our findings and the clinical features of SC, we speculate that the hypermetabolism is a neuroimaging correspondent of persistent clinical features, such as chorea and executive dysfunction, that we described previously in these patients.[26]

Our study has limitations. One of them is that only female patients were included in our sample. Because female sex may be a risk factor for the persistence of SC, our results cannot be generalized to male patients.[14] Another shortcoming is the limited sample size, which weakens the statistical analysis. ■

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