CONCLUSION

SPECT imaging of brain perfusion is more sensitive than EEG and MRI in the evaluation of central nervous system involvement in SLE. In the SPECT findings, cerebral cortices, especially the parietal, temporal and frontal lobes, are the most common sites to be involved in neuropsychiatric SLE patients. Furthermore, with the improvement of SPECT resolution, detection of the deep-seated structure in the brain has become possible. We found that involvement of basal ganglion is also not uncommon while the thalamus and the cerebellum are less involved in neuropsychiatric SLE. In the future, we believe the functional brain SPECT will play an increasingly important role in evaluating CNS conditions in patients with SLE.

REFERENCES

phosphate buffer. The preparation was analyzed for radiochemical purity using previously published procedures (16).

**MATERIALS AND METHODS**

**Radiopharmaceutical**

L,L-ethylcysteinate dimer dihydrochloride was synthesized according to a published procedure (15). Its identity was confirmed by $^1$H and $^{13}$C NMR spectroscopy and mass spectrometry. Technetium-99m-ECD was prepared by reconstitution of a homemade lyophilized labeling kit, containing 0.9 mg ECD.2HC1 and 0.072 mg SnCl$_2$.2H$_2$O, with 1.85 GBq 99mTc in the form of sodium pertechnetate in a volume of 3 ml saline, adjusted to pH 7.4 with phosphate buffer. The preparation was analyzed for radiochemical purity by on September 18, 2016. For personal use only. jnm.snmjournals.org Downloaded from

**Patient Preparation**

The children were allowed to become accustomed to the room for about 15 min with the lights dimmed. Technetium-99m-ECD with a radiochemical purity over 95%, was administered intravenously in a dose of 10–25 MBq/kg. The acquisition was started 10 min later. Young children were sedated 10–15 min after the tracer administration with a cocktail of Largactil and Luminal intramuscularly (both in a dose of 1 mg/kg) and a pentobarbital suppository (dose 30 mg/kg). This caused an extra delay of 15–30 min.

**Acquisition**

The images were acquired with a dedicated brain scanner, a single-slice tomograph with 12 detectors. The scanner has a high sensitivity with a resolution of 6 mm FWHM for 99mTc for the set of collimators used. The patient’s head was positioned parallel to the inferior orbito-mental line and about 8–10 slices were acquired. Slices were acquired sequentially, providing a stack of two-dimensional transaxial images. Acquisition time was 240–300 sec per slice with a relative distance of 10–12 mm. The images were reconstructed with a deconvolution technique and two iterations. Attenuation correction was applied using a best-fitting elliptical contour and constant attenuation coefficient (Chang’s method). The attenuation coefficient was determined with a Hoffman brain phantom.

**Patients**

Between August 1988 and August 1992, all children who were referred for brain perfusion imaging were enrolled. Eighty-eight children had a normal perfusion pattern, as read independently by two experienced nuclear medicine physicians. According to established criteria, the clinical charts were also reviewed retrospectively. The perfusion study was classified as normal if the child fulfilled the following criteria:

1. EEG was normal at time of admission.
2. Brain CT was normal at time of admission.
3. There was no psycho-motor retardation.
4. The clinical follow-up was negative for 1 yr after admission.

Sixteen patients fulfilled the above conditions, 13 boys and three girls. All studied infants were abnormal and none could be classified as normal if the child fulfilled the following criteria:

1. EEG was normal at time of admission.
2. Brain CT was normal at time of admission.
3. There was no psycho-motor retardation.
4. The clinical follow-up was negative for 1 yr after admission.

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2. Brain CT was normal at time of admission.
3. There was no psycho-motor retardation.
4. The clinical follow-up was negative for 1 yr after admission.
TABLE 2

<table>
<thead>
<tr>
<th>Zone</th>
<th>ROI</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemisphere</td>
<td>Both white and gray matter</td>
<td>Hemi</td>
</tr>
<tr>
<td>Cortex</td>
<td>Fronto-medial</td>
<td>FrM</td>
</tr>
<tr>
<td></td>
<td>Fronto-lateral</td>
<td>FrL</td>
</tr>
<tr>
<td></td>
<td>Sensory-motor</td>
<td>Rol</td>
</tr>
<tr>
<td></td>
<td>Temporal</td>
<td>Temp</td>
</tr>
<tr>
<td></td>
<td>Parietal/lateral-occipital</td>
<td>Pa-Oc</td>
</tr>
<tr>
<td></td>
<td>Medial-occipital</td>
<td>OcM</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>Caudate nucleus</td>
<td>NuC</td>
</tr>
<tr>
<td></td>
<td>Lentiform nucleus</td>
<td>NuL</td>
</tr>
<tr>
<td>Thalamus</td>
<td>Hemisphere</td>
<td>Thal</td>
</tr>
<tr>
<td>Cerebellum</td>
<td></td>
<td>Cer</td>
</tr>
</tbody>
</table>

correlation between the AC-PC line on $^{18}$FDG-PET and MR-images, with a deviation of less than 1°. Under normal conditions, this plane through the basal ganglia and thalami easily can be determined on SPECT images.

On the set of standardized brain cuts, regions were drawn manually for further quantitative analysis. Pairs of regions were drawn, as shown in Table 2. The regions of interest (ROIs) were drawn by a technologist with a long experience. Templates were not used, since the size variations with age are considerable. Large ROIs are used for cortex and cerebellum to reduce variability. Frontal and occipital cortex were divided in two, the temporal cortex had one region and the parietal was merged with the lateral occipital. These regions are easy to distinguish and representative examples at two levels are given in Figure 1.

The count density of these regions was analyzed for regional asymmetry. A normalization to the cerebellum or cortex was performed to provide a perfusion index and compare regional uptake between patients. First we calculated the average uptake per ROI over all the image slices, in other words, weighting of the count density to the area involved for each ROI. This provides 11 pairs of values, from which the perfusion indices can be calculated.

Statistics

Results are expressed as the average number of counts per pixel in each region or perfusion index. Left-to-right ratios were computed to evaluate regional changes. Paired Student's t-tests were applied to evaluate the differences between these parameters, and a value of $p < 0.05$ was considered significant. An analysis of variance (ANOVA) was performed on perfusion indices.

RESULTS

In Figures 2 and 3, two typical examples of the final standardized brain perfusion pattern are shown. The images of the younger child (Fig. 2) show a small increase of $^{99m}$Tc-ECD uptake in the basal ganglia when compared to the teenager's images (Fig. 3).

There were no statistically significant differences between similar regions in the right and left hemisphere. Therefore, ipsi- and contralateral ROI results were averaged. The maximum uptake difference between corresponding left and right sided ROIs was 12% and was over 10% in four children on five occasions: three times in Group 1, twice in Group 2 and none in Group 3. In Figures 4 and 5, the results are given for the three age groups after normalization to the cerebellum and cortex, respectively. In both figures, the highest uptake ratio or perfusion index is found for the medial occipital cortex and for the striatum. The influence of age is clearly different for the two normalization methods. Normalization to the cerebellum (Fig. 4) reveals the highest uptake in the medial occipital cortex and basal ganglia of Group 1, and the differences between Groups 1 and 3 are significant. After normalization to the cortex (Fig. 5), the trend with age reverses for the medial occipital zone. The age trend for the striatum remains, but is less pronounced. Note the clear increase of cerebellar uptake, relative to the cortex, with age.
The medial occipital ROI has the highest uptake, except for Group 1 where the striatum is maximal, in part related to the open eyes during 99mTc-ECD injection. See Table 2 for abbreviations.

The ANOVA did not reveal significant changes between left and right hemispheres (p = 0.12). The effect of age group and ROI were both significant after normalization to the cerebellum (p = 0.03 and p < 0.0001, respectively), and the interaction was significant (p < 0.0001). After normalization to the cortex the effect of age group was no longer significant (p = 0.6), whereas ROI still was (p < 0.0001). However, the interaction between age group and region was still significant (p < 0.0001). This analysis corroborates a dependence of age with the regional perfusion pattern observed.

The mean perfusion index and s.d. per ROI, in each hemisphere, are given in Table 3 for the three groups in digits (Table 3) and as graphical displays (Fig. 6), after normalization to the average cerebellar uptake. The perfusion indices of the above selected normal children are used for reference in a database. Thus, perfusion patterns of new pediatric patients can be compared to one of the three available age groups. The medial occipital cortex has the highest index, corresponding to the highest uptake. Relative hyperperfusion of the frontal cortex is seen at older age (Group 3), has the highest index, corresponding to the highest uptake. Relative hyperperfusion of the frontal cortex is seen at older age (Group 3), whereas ROI still was (p < 0.0001). However, the interaction between age group and region was still significant (p < 0.0001). This analysis corroborates a dependence of age with the regional perfusion pattern observed.

The s.d. of the perfusion index for individual ROIs varied between 0.01 and 0.09, in other words less than 10%, except for the caudate nucleus in Group 1 that bilaterally had values of 0.15. Given the small size of these structures at this age and the limited resolution of our system, the effect of the partial volume is the greatest. This caused the largest variations depending on how the structures are 'cut' in the image planes, which is not surprising. Because of the partial volume effect, the actual activity in the basal ganglia is higher in young children as compared to teenagers, amplifying the age trend in perfusion differences. Correction techniques for these effects, however, are cumbersome and complicated and were not available to us.

Matsuda et al. (22) have shown in adults that the perfusion indices obtained with 99mTc-ECD were the same as those obtained with 99mTc-HMPAO, and could easily be converted to CBF values in ml/100 g/min based on 133Xe studies. Thus, CBF measurements with 99mTc-ECD seem feasible.

Although we did not encounter problems with the early start of the acquisition, present knowledge of the biokinetics of 99mTc-ECD suggests that a 10-min delay is too short and an interval of at least 30 min between dose administration and onset of acquisition is recommended (3,5,20). In this series of
patients, such a 30-min delay was present only for Group 1 and other children who needed to be sedated.

CONCLUSION

Technetium-99m-ECD is a safe radiopharmaceutical for brain imaging in pediatric patients. Radiation dose is acceptable and compares favorably to that of other available agents. The perfusion pattern is different for toddlers than for teenagers; younger children have preferential perfusion of the basal ganglia, visual and motor cortex. The age dependence necessitates quantification in order to conclude that the perfusion is normal. A database of perfusion indices with standard deviation is presented for three age clusters.

TABLE 3

<table>
<thead>
<tr>
<th>Group</th>
<th>FroM</th>
<th>FroL</th>
<th>Rol</th>
<th>PaOc</th>
<th>OcM</th>
<th>Temp</th>
<th>NuC</th>
<th>NuL</th>
<th>Thal</th>
<th>Right</th>
<th>FroM</th>
<th>FroL</th>
<th>Rol</th>
<th>PaOc</th>
<th>OcM</th>
<th>Temp</th>
<th>NuC</th>
<th>NuL</th>
<th>Thal</th>
<th>Left</th>
<th>FroM</th>
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<th>NuC</th>
<th>NuL</th>
<th>Thal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 avg</td>
<td>0.997</td>
<td>1.020</td>
<td>1.045</td>
<td>1.021</td>
<td>1.097</td>
<td>0.969</td>
<td>1.098</td>
<td>1.112</td>
<td>1.002</td>
<td>1.001</td>
<td>0.999</td>
<td>0.988</td>
<td>1.112</td>
<td>1.103</td>
<td>0.967</td>
<td>1.089</td>
<td>1.023</td>
<td>1.034</td>
<td>0.984</td>
<td>0.994</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s.d.</td>
<td>0.072</td>
<td>0.062</td>
<td>0.053</td>
<td>0.056</td>
<td>0.048</td>
<td>0.076</td>
<td>0.148</td>
<td>0.060</td>
<td>0.081</td>
<td>0.016</td>
<td>0.016</td>
<td>0.102</td>
<td>0.061</td>
<td>0.148</td>
<td>0.055</td>
<td>0.038</td>
<td>0.046</td>
<td>0.052</td>
<td>0.060</td>
<td>0.075</td>
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<tr>
<td>2 avg</td>
<td>0.942</td>
<td>0.937</td>
<td>0.954</td>
<td>0.923</td>
<td>1.043</td>
<td>0.927</td>
<td>0.998</td>
<td>1.080</td>
<td>0.894</td>
<td>1.004</td>
<td>0.996</td>
<td>0.914</td>
<td>1.038</td>
<td>0.974</td>
<td>0.914</td>
<td>1.015</td>
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<td>0.947</td>
<td>0.910</td>
<td>0.930</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>s.d.</td>
<td>0.063</td>
<td>0.053</td>
<td>0.059</td>
<td>0.060</td>
<td>0.041</td>
<td>0.052</td>
<td>0.050</td>
<td>0.055</td>
<td>0.037</td>
<td>0.017</td>
<td>0.017</td>
<td>0.079</td>
<td>0.065</td>
<td>0.049</td>
<td>0.039</td>
<td>0.047</td>
<td>0.045</td>
<td>0.041</td>
<td>0.070</td>
<td>0.060</td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td>3 avg</td>
<td>0.921</td>
<td>0.871</td>
<td>0.909</td>
<td>0.841</td>
<td>1.002</td>
<td>0.852</td>
<td>0.920</td>
<td>0.925</td>
<td>0.884</td>
<td>0.998</td>
<td>1.002</td>
<td>0.868</td>
<td>0.921</td>
<td>0.959</td>
<td>0.862</td>
<td>0.979</td>
<td>0.840</td>
<td>0.906</td>
<td>0.872</td>
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<tr>
<td>s.d.</td>
<td>0.072</td>
<td>0.091</td>
<td>0.061</td>
<td>0.054</td>
<td>0.054</td>
<td>0.057</td>
<td>0.077</td>
<td>0.061</td>
<td>0.028</td>
<td>0.010</td>
<td>0.010</td>
<td>0.010</td>
<td>0.091</td>
<td>0.063</td>
<td>0.045</td>
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</table>

The values are given for each hemisphere of the three age clusters. Data are ordered in a cyclical way: cortical, basal ganglia, thalamus, cerebellum and reversed. Normalization was done to the average cerebellar count rate. See Table 2 for abbreviations.
Brain Perfusion SPECT in Lyme Neuroborreliosis

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Departments of Nuclear Medicine and Psychiatry, Kanazawa University School of Medicine, Kanazawa, Japan

SPECT imaging brain perfusion using ⁹⁹mTc-HMPAO was performed on a 38-yr-old woman with Lyme neuroborreliosis confirmed by autopsy. The patient had been suspected of spinocerebellar degeneration. Cerebral blood flow was diffusely decreased throughout cerebral cortices but cerebellar blood flow was not impaired, which indicated that the diagnosis was unlikely spinocerebellar degeneration. These findings suggested that brain perfusion SPECT provides useful information in diagnosing the patients with Lyme neuroborreliosis, especially when spinocerebellar degeneration is included in the differential diagnosis.

Key Words: Lyme neuroborreliosis; SPECT; HMPAO; spinocerebellar degeneration

J Nucl Med 1997; 38:1120-1122

Lyme disease is a multisystemic disease caused by tick-borne spirochete Borrelia burgdorferi, and its invasion into the central nervous system develops a diversity of neurologic and psychiatric disturbances (1,2). In Lyme disease, the central nervous system involvement usually becomes involved in the second stage showing meningitis, multiple cranial nerve palsies, motor or sensory radiculoneuritis and polyneuropathy. In more severely affected cases, disseminated cerebrolyelitis, leukoencephalitis and demyelinating encephalopathy have been found, which characterize the third stage of Lyme disease, known as Lyme neuroborreliosis (LNB). Findings in imaging studies with brain CT and MRI are frequently subtle and nonspecific (3,4). This article describes previously unreported HMPAO-SPECT findings in a patient with LNB.

CASE REPORT

A woman, who had been in good health, became aware of unstable walking at 37 yr. She had not experienced any signs or symptoms of skin lesion or joint pain. She consulted a general hospital and was neurologically examined, but no abnormality was detected. However, her neurological symptoms gradually developed. Her gait became definitely ataxic, and she could not stand up for a long time. She had choreothetotropic movement in her upper extremities, spoke explosively and had dysdiadochokinesis. Five months later, she could not stand up and memory disturbance became evident with inertia, and she was admitted to our hospital.

Neurological examination disclosed marked disturbance in coordination and dysmetria including intentional tremors. She was frequently drowsy, restless and disoriented as to time and place. She responded very slowly to any questions. No meningeal signs were detected. Mini-Mental State Examination score was 16/30 (5). Her ocular movements had limitation on upward and downward gaze. Her pupil was miotic but reactive. She was judged to have supranuclear bulbar palsy because of the absence of pharyngeal reflex. She had muscle weakness detected in general skeletal muscles that were hypotonic. Chorea-thetotropic movements were present in her upper and lower extremities. Deep tendon reflexes

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We thank Yolande Peeters for her dedication in taking care of the scanner, performing the studies and drawing the regions. The help of Karl Syndulko, PhD with the statistical analyses is greatly appreciated.

REFERENCES


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Normal Brain Perfusion Pattern of Technetium-99m-Ethylcysteinate Dimer in Children

Christiaan Schiepers, Alfons Verbruggen, Paul Casaer and Michel De Roo


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