

Single-photon Emission Tomography (SPECT) in
the Study of Aphasia: A Preliminary Report

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In the past decade considerable enthusiasm has been generated for the study of brain function by means of single-photon emission tomography (SPECT) (Ackerman, 1984; Metter, 1985). SPECT provides three-dimensional representations of regional cerebral blood flow (rCBF) noninvasively with relatively low radiation doses and modifications of conventional nuclear medicine equipment.

Studies of brain pathophysiology in vivo are of particular importance in the study of aphasia. Employing ^{18}F FDG positron emission computed tomography, Metter (1984) and his associates have demonstrated areas of metabolic depression larger than the area of infarction shown on conventional CT in aphasic patients. This group suggested that brain and language theory based solely on structural damage needs modification to account for the metabolic changes observed in their patients.

For most institutions the cost to set up a PET scanner is prohibitive because of the need for a cyclotron and the expensive scanner cost. SPECT utilizes a relatively inexpensive scanner, needs no cyclotron or fast chemistry and provides regional blood perfusion much the same as PET. Although SPECT studies are just beginning, preliminary reports have shown the procedure to be particularly applicable for the study of stroke (Bonte and Stokely, 1981; Bonte, Stokely, Devous and Ross, 1983; Hill, Magistretti, Holman, *et al.*, 1984; Lassen, Henriksen and Paulson, 1981). Studies with acute stroke patients using either Xenon-133 inhalation or I-123 Iodoamphetamine (IMP) as the tracer have shown that changes in tracer distributions could be identified even when conventional CT scan was normal (Bonte and Stokely, 1981; Bonte, *et al.*, 1983; Devous, Stokely and Bonte, 1985; Hill, *et al.*, 1984; Lassen, *et al.*, 1981). Although blood flow may not be a clinically meaningful parameter by itself, it is an epiphenomenon, indirectly reflecting disturbed metabolism (Ackerman, 1984).

Tikofsky, Collier, and Hellman, *et al.* (1985), reported on five aphasic patients using the IMP SPECT technique during the resting state. This report of chronic aphasia found some association between improved rCBF and recovery as measured by the Western Aphasia Battery. The purpose of the present report is to (1) describe the 133-Xenon SPECT procedure and instrumentation; and (2) to present case illustrations of three aphasic patients with diverse clinical profiles evaluated in our laboratory by SPECT, CT and language measures.

Background

Although cerebral blood flow is a basic biological process, the clinical significance of disturbed patterns and measured flow has confounded investigators. Two-dimensional techniques, despite considerable investment of time and money, produced relatively little information that proved to be of clinical value (Ackerman, 1984). Two-dimensional systems were limited in that they reflected changes in flow only on the brain surface, counts from the contralateral hemisphere were found to contaminate results, and Xenon scatter from the nasal passages often produced artifactual data (Ackerman, 1984). Lassen and his colleagues thus decided to construct a device that would provide three-dimensional representations of rCBF. Working with Stokely, Sveinsdottir and Rommer (1980), the group designed a single-photon emission computed tomograph (SPECT) capable of deriving and displaying regional cerebral blood flow.

The SPECT Procedure

The SPECT instrument used in our laboratory is the one developed by Stokely *et al.* (1980). It is a Tomomatic 64 made by Medimatic in Copenhagen, Denmark. This unit and its operation have been described in detail by Bonte and Stokely (1981). Briefly, it consists of four detector arrays mounted in a hollow configuration that rotates around the subject's head at 6rpm. Special focused collimators define three transverse tomographic sections with centers 4 cm apart. Xenon is administered in an air/oxygen mixture by inhalation during the first minute of a 4-minute washout procedure. The patient breathes room air during the remaining 3 minutes of the study. Three tomographic sections are generated at 2, 6, and 10 cm above and parallel to the canthomeatal line. rCBF (measured in milliliters per minute per 100 grams of tissue) is calculated within each pixel by the method of Kanno and Lassen (1979) and displayed quantitatively in a 16-shade black and white or color scale. System resolution (as measured with a Xenon line source in water) varies from 1.7 cm in the center of each slice to 1.0 cm at the edge transversely. rCBF images are scaled, rotated and translated to match a pre-determined standard brain outline that includes a graphic overlay that automatically figures regions of interest defined from a CT cross section. This includes frontal, prefrontal, temporal, parietal and occipital areas, as well as central areas from both hemispheres using slice 2, 6 cm above the canthomeatal line.

In our laboratory control studies have been carried out on 98 normal subjects and 8 subjects with language activation probes. Test-retest reliability from one hour to 10 days has been reported by Devous, Stokely, Chehabi and Bonte (1986).

Case Reports

Case 1. A 20-year-old right-handed woman with history of hypertension and migraine had sudden onset of mild hemiparesis and nonfluent aphasia as determined by the Boston Diagnostic Aphasia Examination (Goodglass and Kaplan, 1972). CT scan showed a very small frontal lesion. At a follow-up examination two years later, the patient continued to have a moderately severe nonfluent aphasia and motor deficits. CT scan remained unchanged, yet SPECT

rCBF demonstrated reduced flow in most of the left hemisphere, including Wernicke's area and the parieto-temporal junction. This study demonstrates cortical dysfunction as determined by rCBF in areas remote from the primary lesion as other investigators have found with metabolic and electrophysiological techniques (Metter et al., 1984; Nagata, Tagawa, Shishido, and Uemura, 1986).

Case 2. A 56-year-old ambidextrous man was admitted to the hospital with right hemiparesis and a neurologist's diagnosis of global aphasia. CT scan at the time of admission revealed low density areas in the left temporal, inferior parietal, and occipital areas and less well-defined areas in the left frontal region. Arteriography revealed some small vessel disease distally and left carotid ulcerated plaque. Upon discharge the physician's report stated that the patient had made remarkable recovery with minimal paresis and significant return of communication skills. Six weeks after discharge the patient was studied with SPECT for determination of potential appropriateness of carotid endarterectomy. Presurgery SPECT showed profoundly low flow throughout the left temporal lobe. Postsurgery SPECT, four weeks after surgery, showed improvement in rCBF but no increase in focal uptake in tissue to which language or cognitive changes could be attributed. This was supported by pre- and postsurgery language testing which revealed no significant change in language status. This is in agreement with other investigators who have not documented changes in cognitive and language function following endarterectomy.

Case 3. A 65-year-old strongly right-handed man with history of right hemisphere infarction was seen 10 years post onset. At the time of study, the patient had left hemiparesis, hemisensory loss, and crossed aphasia with moderate comprehension deficits and nonfluent speech as determined by the Boston Diagnostic Aphasia Examination. CT scan revealed a large area of infarction in the territory of the right middle cerebral artery, including areas homologous to Broca's and Wernicke's areas, extensive involvement of subcortical white matter, and portions of the basal ganglia. The left hemisphere showed no abnormalities. SPECT rCBF study obtained during the resting state correlated with the CT scan. Blood flow in the left hemisphere was normal. In addition, rCBF determinations were made during several activation procedures. Task specific increases in rCBF were found when the subject was doing math problems, the WAIS Information subscale, and phoneme detection tasks. While flow pattern changes from resting state on the WAIS subscale could be attributed to attending or alerting responses, the uptake in right temporal lobe during math activation and bihemispheric frontal increases during the phoneme task represent task specific focal changes in rCBF.

Summary

Our present experience with SPECT in cerebral vascular disease suggests that it has clinical importance for detecting important changes in rCBF before development of positive CT and that areas of decreased blood flow at a distance to the infarct can be demonstrated. SPECT also has clinical utility for pre- and post-operative analysis of rCBF. SPECT has research potential for assessing brain function related to brain and language theory and for the study of language recovery.

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DISCUSSION

- Q: Why do you only take one slice, instead of multiple slices?
- A: The machine that you have in Iowa provides five slices, but on the machine that we use only 3 slices are obtained. We do not get that much information from slice 1 and 3. We sometimes look at slice 1 but in terms of language function, the primary information is out of slice 2.
- Q: You did not follow these people up in recovery? Do you show that people who recover language have a certain pattern of blood flow?
- A: We are just starting to follow people serially. The patients we have followed up to this point in time have all been chronic patients.
- Q: Most of us are going to have access to CT scan information and we will be fortunate if we have that. Is there anything that we can predict yet from this research, from the size or location of lesions, visualized on CT scans? Can we make any kind of predictions about metabolic depression and how that is going to impact upon prognosis?
- A: (Walker-Batson) I would say in terms of prognosis, that we have not run enough people serially to know what is meant with resting blood flow. Ron Tikofski has run a few people and with five subjects, he thought he saw a difference in resting state blood flow with improvement on the Western Aphasia Battery. That has not been my experience. People that we don't think will get better based on their blood flow patterns have gotten better. Then you see patients like Case 1, that you would have predicted based on their CT would have gotten better and they don't. So I'm not really sure, I think certainly with the SPECT technique that we are going to need to do more language activation. We've spent about 2 years and \$20,000 developing a phoneme detection task that is unilateral to those left prefrontal areas. I think we're seeing people who have difficulty with that, I'm very interested in the prefrontal areas and prediction for recovery but I haven't looked at enough patients to know yet. That is what I want to look at. In terms of just looking at a CT, I don't think we know enough. I do think more institutions are going to use SPECT scanners because they're going to be less expensive and I think you will have access to them just like CT scans. We have also run four patients with magnetic resonance spectroscopy and we have found differences in phosphate metabolism that we could not have predicted.
- C: If the patient is aphasic they have temporal-parietal depressed metabolism. That will be true whether or not you see anything on CT scans. That's been my experience. If you see structural lesions in Marie's quadrilateral space that are at least of moderate size and involve the anterior internal capsule and at least part of the posterior internal capsule, my presumption is you will see prefrontal hypometabolism and if you see structural damage involving the genu of the internal capsule or into the posterior part of the internal capsule in somebody with a pure subcortical lesion you will see a Broca's aphasic. And that's based on data I didn't present today. So as far as prognosis that's a tough question.
- C: A couple of years back we used a modified standard CT scanner and got similar kind of pictures. It's clear that SPECT is cheaper but there

are several other ways to get the same kinds of information. BEAM, evoked potential approaches used with electroencephalography or magnetoencephalography can give us similar kinds of information. These procedures are now appearing everywhere and may truly prove to be helpful from a diagnostic and even treatment point of view.

- C: (Walker-Batson) I think electrophysiological information is very important. We hope to couple BEAM with the SPECT to see the differences that we would get. Again in terms of cost effectiveness, at least in our locale, BEAM is about \$500.00, SPECT is \$450.00, so it's about the same cost range.
- Q: What's your normal range of blood flow?
A: In each hemisphere?
- Q: Yes, in normal subjects.
A: The left is 69 with a standard deviation of about 4; the right is 71.
- Q: On that case with the endarterectomy, what brought the entire right hemisphere up? Did that individual have hyperperfusion on the right side?
A: Yes, he did. We did a Diamox study in addition to the slide that I showed and this was the indication for the surgical intervention. He definitely had cerebral vascular disease.
- Q: Did they do a follow-up SPECT on him?
A: Well, we had planned to follow this patient serially and he had another stroke.
- Q: What do you make of the performance of that unfortunate 20-year-old patient with the small lesion on CT and the apparent massive disruption of perfusion on SPECT? Did I hear you say something about effects at a distance?
A: Well, I chose this case to demonstrate the kind of discrepancies you can get between CT and perfusion or metabolic studies and this is probably one of the most dramatic ones we have seen in the last five years -- to have such a tiny lesion and be so wiped out. Also she was 20 years old so we thought she would do well and we wondered why she had not.
- C: When we draw our imaging and behavioral correlations and do our analyses, we've got to be able to accommodate patients like that one as well as those that fit so nice and smoothly into our theory.
A: Absolutely. We have seen patients that absolutely we would have predicted -- one I think of that had absolutely no left hemisphere usable perfusion. It was like an embolic shower, of posterior, middle, and anterior arteries. What could we have predicted? You know, he should not be walking around. I think these kind of outliers don't fit the model.
- Q: Do you have a risk history?
A: Well, that patient (Case 1) had a history of hypertension. I have just interacted with this patient once. She was seen by Elliot Ross before I came to the laboratory. We do see patients like this whose blood flow is much more disrupted than would have been predicted by the CT scan but his is probably the most dramatic example.