Epilepsy surgery improves regional glucose metabolism on PET scan

A case report

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Summary. A patient with medically intractable complex partial epilepsy was evaluated for epilepsy surgery by electroencephalograph recording with depth electrodes and 18F-fluorodeoxyglucose positron emission tomography (PET). A small calcified arteriovenous malformation was excised from the left parietal lobe, and the patient became seizure free. Baseline and language stimulation PET scans were obtained preoperatively and 10 months postoperatively. There was a significant increase in glucose metabolism of the left temporal lobe postoperatively, which we interpret as evidence of improved neuronal function. We suggest that this case represents evidence for a functional, and reversible, inhibition of neuronal metabolism by epileptic activity.

Key words: Complex partial epilepsy – Positron emission tomography – 2-Deoxyglucose – Epilepsy surgery

Introduction

The surgical treatment of medically intractable complex partial epilepsy has been available since the turn of the century [11,17]. In addition to the obvious benefits such surgery provides the patient, the pre- and postsurgical, multidisciplinary diagnostic evaluations have contributed important basic information about epilepsy. One of the more recently developed tools to evaluate these patients is positron emission tomography (PET) of the brain. PET using 18F-2-fluoro-2-deoxyglucose (2-FDG) is able to measure local cerebral glucose utilization in humans. In patients with complex partial epilepsy, 2-FDG PET performed interictally has frequently revealed areas of hypometabolism which have correlated with the ictal focus [9]. The etiology of this hypometabolic zone is still unclear despite human and animal experiments.

There are two current hypotheses to explain this hypometabolism, and they are not mutually exclusive [9]. One suggests an anatomical substrate such as loss of dendritic spines and synapses. The other suggests a functional substrate related to inhibition or inactivation of healthy neuronal elements by the epileptic process. A functional etiology could be reversible if the epilepsy were controlled. However, no studies have been able to test this hypothesis because either the epilepsy is medically intractable or control is obtained by surgically removing the area of hypometabolism. Once the tissue is removed, a follow-up PET scan would be meaningless. Nevertheless, there is indirect evidence supporting a functional etiology. First, these hypometabolic zones can become hypermetabolic during a seizure [9]. Second, a patient has been reported with Lennox-Gastaut syndrome in whom a hypometabolic temporal lobe returned to normal following commissurotomy and clinical improvement [6]. Third, a case has been described of complex partial epilepsy with a right occipital focus and right occipital and temporal hypometabolism which improved when the patient was seizure free [4,9].

We present a case of complex partial epilepsy which addresses the hypothesis of a functional etiology for epilepsy-induced regional hypometabolism. We employed a strategy of baseline and language stimulation PET scans to enhance our ability to uncover a lesion that could be functionally silent under baseline conditions, as suggested by Mazziotta and Engel [9].

Materials and methods

18F-2-FDG was prepared by the method of Tewson [15] from 18F-fluoride, produced on the University of Wisconsin EN tandem Van de Graaff. The Tewson synthesis is known to result in 2-FDG without contamination with 18F-fluoro-deoxymanose. Head contour and attenuation correction in the data planes were defined with a transmission source prior to each study. Forty minutes following the intravenous administration of 2-FDG, three cross-sectional images were obtained with an ECAT-II tomograph (EG + G Ortec) at 3, 4.5 and 6 cm above the orbitomeatal line. These sections will be referred to as low, middle and high, respectively. The preoperative scans used shadow shields producing a resolution of 1.7 cm full width at half maximum (FWHM). Postoperatively, we used shields which allowed for a 1.3 cm FWHM because of the availability of more isotope. Glucose utilization rates were computed according to the method of Hutchins et al. [7].

Data were transferred to a Gamma 11 system for analysis. Homologous left-right regions were outlined to include frontal, temporal and parietal cortex. The ratio of the region of interest/whole slice mean was calculated for each slice and then averaged to yield a final dimensionless value for each brain area. These values are presented in Table 1, and the left/right ratio is calculated from these averages.
Informed consent was obtained for the PET scans. Preoperatively, a baseline scan was obtained, followed 4 days later by a language stimulation scan. The patient did not have any seizures during this interval. Ten months postoperatively, a baseline and language stimulation scan were obtained separated by 1 day. The patient had been seizure free for the preceding 6 months. The patient was on long-term phenytoin and carbamazepine during both pairs of PET scans. A protocol was devised to evaluate the effect of language on glucose metabolism which would both maximize attentiveness and minimize memory requirements.

**Language stimulations.** Language stimulation was provided with a tape-recorded list of 150 single words presented binaurally through earphones at a rate of 2/min. The stimuli were randomly selected from the Thorndike and Lorge list of most frequently occurring words. These words were then taped-recorded in random order so that they occurred at a rate of 2/min for 50 min. Interstimulus intervals were also determined randomly so that within each minute one word would appear any time between 1 and 25 s and the second word would appear any time between 30 and 55 s. The first ten were used as orientation and practice stimuli and the rest as experimental stimuli.

Prior to actual testing the patient was told he would be blindfolded and fitted with a pair of earphones, and that he would then hear a list of words presented to both ears. He was told his task was to elevate his left and right index fingers simultaneously each time he heard a word containing the /s/ sound. He recognized the difference between the “s” letter and the /s/ sound and understood that his task was to identify only the sound. The grapheme-phoneme difference was emphasized so that the task involved phonemic or sound analysis, which is primarily a left or dominant hemisphere task, rather than grapheme analysis, which may be more of a function shared by the two hemispheres. The patient was then positioned in the scanner, re-instructed as to the task, and then fitted with the eyepatch and earphones. Next, the ten sample items were presented binaurally to determine the most comfortable loudness level for stimulus presentation and to guarantee that the patient understood the task.

Presentation of the test stimuli began 10 min before injection and then continued for 45 min. The patient’s responses were entered on an answer sheet by one of the experimenters, who also monitored the patient’s attention to the task and roused him if his concentration waned. The patient made only three mistakes during each of the language stimulation procedures, which was within normal limits.

**Baseline.** In the baseline condition the patient was told that he would periodically be touched on both arms and that he was to respond by simultaneously elevating his left and right index fingers. He was then positioned in the scanner, wearing a blindfold and earphones, and was re-instructed. Next he was stimulated ten times at irregular intervals and at a rate of 2/min to guarantee that he understood the task. Tactile stimulation and the index finger response were selected because non-linguistic stimulation with the same kind of patient response as in the language stimulation condition was required.

Tactile stimulation at the rate of 2/min began 10 min prior to injection and continued for 45 min after injection was complete. The experimenter roused the patient, if he failed to respond to each touch, by raising his index fingers.

**Case report**

**Seizures**

This 37-year-old, right-handed shipping clerk had had complex partial epilepsy for 16 years. His seizures varied from none to several a week and were refractory to phenytoin, phenobarbital, primidone, carbamazepine, valproic acid and methsuximide. Many of his seizures were preceded by a blank stare, while others started with hyperextension of his neck and closing his eyes. He frequently turned to the left and flexed his extremities. This was followed by automatisms (not all were present during each seizure) including the following: picking with his hands, rocking, spitting and smearing the spit with his hands, masturbation with and without ejaculation. The patient was amnesic for these events.

**Past medical history**

The patient had no medical problems. The findings of a neurologic examination were normal and his full-scale IQ was 103. Three years prior to his epilepsy surgery, a CT scan had revealed a small calcified lesion in the floor of the lateral wall of the left ventricular atrium. An arteriogram was normal.

**Language profile**

The patient was first evaluated for speech and language pathology 3 years prior to his epilepsy surgery. At that time and at all subsequent evaluations, he was given a standard language battery consisting of: the Mayo Clinic procedures for language evaluation (unpublished), and adaptation of Schuell’s short examination for aphasia [13], Token test [3], word fluency measure [1], Boston naming test [5], reading comprehension battery for aphasia [8], Raven’s coloured progressive matrices [12] and a standard speech sample [18] to elicit spontaneous and imitative speech and reading aloud.

**Phase I evaluation**

The patient’s neurologic examination, CT scan, full-scale IQ and language function had not changed over the last 3 years. His speech-language profile was most consistent with an anomic aphasia. Deficits in auditory and reading comprehension were mild and consisted primarily of delayed but correct responses rather than outright errors. Scalp EEG with closed-circuit video monitoring confirmed the etiology of the patient’s spells as being complex partial seizures which started in the left hemisphere.

**Phase II**

The patient had depth electrodes (Rhodes Medical Co., California) stereotaxically implanted under CT guidance into the orbitofrontal, hippocampal and amygdala regions bilaterally. Spontaneous seizures were seen first in the left hippocampus and amygdala electrodes and then spread to other areas. Epileptiform activity never started in the frontal electrodes. No clinically silent electrographic seizures were ever recorded from any of the six electrodes. Moreover, the electrographic seizure was delayed by as much as 40 s from the onset of the clinical seizure. This suggested that the ictal focus was not at the recording sites. Afterdischarge threshold testing revealed a higher threshold in the left hippocampus compared with the