Single-voxel proton MR spectroscopy and positron emission tomography for lateralization of refractory temporal lobe epilepsy.

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Single-Voxel Proton MR Spectroscopy and Positron Emission Tomography for Lateralization of Refractory Temporal Lobe Epilepsy

Eric Achten, Patrick Santens, Paul Boon, Danny De Coo, Tom Van De Kerckhove, Jacques De Reuck, Jacques Caemaert, and Mark Kunnen

PURPOSE: We compared the metabolic information obtained from single-voxel proton MR spectroscopy and positron emission tomography (PET) in patients with temporal lobe epilepsy.

METHODS: Twenty-nine patients with temporal lobe epilepsy were screened for metabolic abnormalities with both proton MR spectroscopy and PET. Lateralization with MR spectroscopy was possible by using NAA/(Cho+Cr) and an asymmetry index. Hypometabolism as determined by PET was classified as typical or complex.

RESULTS: Twenty-four (96%) of 25 patients whose seizure onset could be lateralized to one temporal lobe showed ipsilateral lateralization with either MR spectroscopy or PET, whereas concordant lateralization with both techniques was possible only in 14 (56%) of the 25 patients. MR spectroscopy showed 42 abnormal temporal lobes whereas PET showed only 25 lobes with decreased metabolism. All temporal lobes with hypometabolism at PET also had a low NAA/(Cho+Cr). Five patients (20%) with negative PET studies had seizures lateralized correctly with MR spectroscopy.

CONCLUSION: Proton MR spectroscopy is more sensitive in depicting metabolic abnormalities than is PET in patients with temporal lobe epilepsy. Patients with negative PET studies will benefit from MR spectroscopy for the purpose of lateralization.

Although many patients with so-called cryptogenic temporal lobe epilepsy have anomalies that can be depicted by using an optimized magnetic resonance (MR) imaging protocol (1), in some cases, lateralization with electroencephalography (EEG) and MR imaging is not accomplished easily. Neuropsychological examination and metabolic tests, such as positron emission tomography (PET), single-photon emission computed tomography (SPECT) (2), and MR spectroscopy (3), may be used to corroborate localizing results. The invasive intracarotid amytal procedure gives information about language location and memory support (4), and depth electrode studies are required when noninvasive presurgical tests produce conflicting results (5). Improving noninvasive diagnosis will diminish the need for invasive procedures.

Both single-voxel proton MR spectroscopy (6–11) and fludeoxyglucose F 18 positron emission tomography (FDG-PET) (12–20) are metabolic screening techniques that are used in the presurgical examination of patients with refractory temporal lobe epilepsy. Recent studies have shown that N-acetylaspartate (NAA) (3, 6–9) is often decreased in the temporal lobes of patients with temporal lobe epilepsy, and that variable changes in choline (Cho) and creatine/phosphocreatine (Cr) concentrations have also been reported (3, 9–11) (G. Ende, K. D. Laxer, R. Knowlton, et al, “Quantitative 1H SI Shows Bilateral Metabolite Changes in Patients with Unilateral Temporal Lobe Epilepsy with and without Hippocampal Atrophy,” presented at the annual meeting of the Society of Magnetic Resonance in Medicine, Nice, France, August 1995; C. O. Duc, D. Meier, X. G. Golay, et al, “Investigation of Temporal Lobe Epilepsy by Quantitative 1H MRS of the Hippocampus in Vivo,” presented at the annual meeting of the Society of Magnetic Resonance in Medicine, Nice, France, August 1995). Because absolute quantification remains difficult, the NAA/(Cho+Cr) or the NAA/Cr ratios, or the normalized value for NAA, are usually calculated (9–11, 21) (Ende et al, “Quantita-
negative..."). Duc et al, “Investigation...”). We have intro-
duced the use of an asymmetry index in conjunction
with NAA/(Cho + Cr) to improve the lateralizing ca-
pacity of MR spectroscopy (3) (Table 1).

Interictal PET findings can regionalize zones of
interictal metabolic dysfunction related to the focus
of partial epilepsy (12–20). Several reports indicate a
60% to 90% prevalence of temporal lobe hypometab-
olism in patients with medically refractory mesial
temporal lobe epilepsy (14–17, 19). In this study, we
compared MR spectroscopy and PET as to their ef-
effectiveness in lateralizing seizure focus, and we hy-
pothesized a possible relationship between the meta-
bolic abnormalities depicted.

**Methods**

**Clinical and EEG Assessment**

Twenty-nine consecutive patients (age range, 14 to 53 years)
with symptoms of temporal lobe epilepsy refractory to medical
treatment and with no tumors or vascular malformations, tra-
matic lesions, or neuronal migration disease were entered into
a presurgical evaluation program (5). All patients underwent a
clinical neurological examination and several scalp EEGs. Ha-
bital complex partial seizures were recorded during prolonged
video-EEG monitoring (Beehive and SZAC 32-channel digital
EEG, Telefactor, West Conshohoken, Pa). Lateralization was
attempted by using the EEG and clinical data.

**Interictal MR Imaging and Proton MR Spectroscopy**

MR imaging of the temporal lobes was performed on a
clinical 1.5-T system. The temporal lobes and the hippocampal
structures were examined on oblique coronal TI-weighted in-
version recovery images, and the volumes of the hippocampus
and amygdala were calculated from oblique coronal three-
dimensional magnetization-prepared rapid gradient-echo im-
ages with a manual ray-tracing method (1). Single-voxel proton
MR spectroscopy was carried out immediately after MR imag-
ing using a 8-mL voxel (20 20 20 mm3) positioned over
the mesotemporal lobe, including part of the hippocampus (Fig
1). The signal over the voxel of interest was shimmed to within
the field of view was 40 mm above this orbito-

P

**PET Scanning and Evaluation**

All PET studies were performed in a dimly lit room, with the
patients’ eyes open and ears unplugged. After a minimum
4-hour fast, patients were positioned in the gantry so that
scan-plane orientation was parallel to the orbitomeatal line
and the center of the field of view was 40 mm above this orbito-

N

Results

From the extracranial EEG recordings (interictal
and ictal), 24 of 29 patients with temporal lobe epi-
FIG 1. Standard positioning scheme of the mesotemporal voxel of 8 mL on three orthogonal images through the temporal lobe. A–C, Axial T2-weighted image (2370/80/1 [repetition time/echo time/excitations]) (A), coronal half-Fourier T1-weighted image (300/15/1) (B), and sagittal half-Fourier T1-weighted localizer image (300/15/1) (C). Care is taken to stay clear of the tip of the temporal bone to avoid shimming problems. Standardization diminishes partial volume bias due to differences in white and gray matter content in the voxel.

D. In the spectrum (1600,135,256) from the normal right temporal lobe of one patient (case 9), three peaks can be recognized: from right to left: NAA at 2 ppm, Cr at 3 ppm, and Cho at 3.2 ppm.

FIG 2. Case 9: patient with seizure onset lateralized to left temporal lobe by EEG studies. The inversion-recovery T1-weighted MR images (3500/20/1; inversion time, 300) (not shown) depicted hippocampal sclerosis on the left side as the only imaging abnormality. The spectrum (1600/135/256) shows a low NAA/(Cho+Cr) on the left side only (A), and the PET scan (ECAT IV camera) (B) has a typical diffuse hypometabolic focus in the left temporal lobe (arrows). A modified left temporal lobectomy was performed, and the patient remains seizure free after 36 months.
lepsy were considered to have lateralized focal meso-
temporal seizure onset; one patient (case 2) had re-
gional frontotemporal onset from one side; and one
patient (case 16) had bilateral independent epileptic
activity. In three patients (cases 12, 22, 26), seizure
onset could not be lateralized. Table 2 summarizes
the test results for all patients.

When using our optimized MR imaging protocol in
the group of 25 patients who showed lateralized sei-
zure activity on the EEG examination (Table 2), we
found that 22 (88%) had either hippocampal (n = 14)
or mesial temporal (n = 8) sclerosis on the same side.
One subject (case 28) had no abnormal imaging find-
ings, and two (cases 17 and 19) had bilateral symmet-
tric hippocampal damage. MR spectroscopy lateral-
ized seizure onset correctly in 19 (76%) of 25 patients,
and no discordance with the EEG findings was noted.
PET also showed concordantly lateralized hypome-
tabolism in 19 patients, also with no discrepancies
regarding the EEG. On the other hand, seizure onset
was lateralized concordantly with either MR spectro-
copy or PET in 24 (96%) of the subjects, but in only
14 (56%) of the subjects with both techniques (Fig 2,
Table 3). One of the patients with bilateral symmetric
hippocampal damage (case 17) had bilateral symmet-
ric low NAA/(Cho+Cr) values but had seizure onset
lateralized with PET only, whereas the other patient
(case 19, Fig 3) had seizure onset lateralized with
both MR spectroscopy and PET. One patient with
temporal lobe epilepsy and no MR imaging abnor-
malities (case 28) had normal values at MR spectros-
copy and a normal PET scan.

Bilaterally low NAA/(Cho+Cr) ratios were found
in 10 of 25 patients with temporal lobe epilepsy and
lateralized seizure onset at EEG (Table 3); in six
patients, seizures could further be lateralized with the
asymmetry index, and the other four had symmetrically
low NAA/(Cho+Cr) values. A classical, ipsilateral,
diffuse temporal lobe hypometabolism was depicted
by PET in nine of these subjects, and only one (case
6) also had bilateral PET hypometabolism but worse
on the side ipsilateral to that depicted at EEG.

Six patients with lateralized temporal lobe epilepsy
had normal findings at PET; four with the ECAT IV
scanner (cases 4, 10, 18, and 28) and two with the ECAT 951/31 (cases 27 and 28). In five of these six patients, MR spectroscopy lateralized seizure onset ipsilateral to the side depicted by EEG and MR imaging. Of these five patients, three (cases 4, 10, and 27) had only hippocampal sclerosis at MR imaging whereas two (cases 18 and 25) had signal changes in the anterior temporal lobe in addition to hippocampal sclerosis.

To date, a final decision concerning surgery has been reached in 23 of the 25 patients with lateralized temporal lobe epilepsy (Table 2): 17 have had surgery and two are scheduled for surgery in the near future. Depth electrode studies showed regional rather than focal onset in two patients (cases 2 and 13) and these patients were not operated on; one patient (case 4) refused surgery, and one patient (case 10) could not be operated on because of discrepant results in the intracarotid amytal procedure (3). Among those who had surgery, two patients (cases 18 and 25) had ipsilateral abnormalities at MR spectroscopy and no FDG hypometabolism, and five patients (cases 6, 15, 17, 20, and 29) had ipsilateral FDG hypometabolism and nonlateralizing MR spectroscopic values. In two patients (cases 19 and 28), no consensus was reached.

Pathologic examination showed clear signs of sclerosis in all patients who went to surgery. The quantitative correlation between the MR spectroscopic or PET data and the severity of the pathologic changes was not examined.

The patients with nonlateralized refractory epilepsy (four of 29; cases 12, 16, 22, and 26), none of

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex/Age, y</th>
<th>EEG</th>
<th>MR Imaging</th>
<th>PET Hypometabolism</th>
<th>PET Camera</th>
<th>Consensus Surgery</th>
<th>Side</th>
<th>Outcome</th>
<th>Follow-up, mo</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>M/21</td>
<td>L meso TL</td>
<td>L HCS</td>
<td>L</td>
<td>Complex: L hemisphere</td>
<td>951 L</td>
<td>Scheduled for surgery</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F/28</td>
<td>L FTL</td>
<td>L meso TL</td>
<td>L</td>
<td>Diffuse: L TL</td>
<td>IV L</td>
<td>Depth electrode study:</td>
<td>L regional onset</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F/19</td>
<td>R meso TL</td>
<td>R HCS</td>
<td>R</td>
<td>Complex: R hemisphere</td>
<td>IV R</td>
<td>1A</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F/26</td>
<td>R meso TL</td>
<td>R HCS</td>
<td>R</td>
<td>None</td>
<td>IV R</td>
<td>Refused surgery</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F/31</td>
<td>R meso TL</td>
<td>R meso TL</td>
<td>Bi R</td>
<td>Diffuse: R TL</td>
<td>IV R</td>
<td>1A</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F/36</td>
<td>R meso TL</td>
<td>R HCS</td>
<td>Bi</td>
<td>Complex: R &gt; L TL</td>
<td>IV R</td>
<td>1A</td>
<td>18</td>
<td></td>
</tr>
<tr>
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<td>R HCS</td>
<td>R</td>
<td>Diffuse: R TL</td>
<td>951 R</td>
<td>Recent surgery, no seizures</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M/39</td>
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<td>L meso TL</td>
<td>L</td>
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<td>IV L</td>
<td>1A</td>
<td>24</td>
<td></td>
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<tr>
<td>9</td>
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<td>L HCS</td>
<td>L</td>
<td>Diffuse: L TL</td>
<td>IV L</td>
<td>1A</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>M/18</td>
<td>L meso TL</td>
<td>L HCS</td>
<td>L</td>
<td>None</td>
<td>IV L</td>
<td>Discrepant IAP, not operated on</td>
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<td></td>
</tr>
<tr>
<td>11</td>
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<td>L meso TL</td>
<td>Bi L</td>
<td>Diffuse: L TL</td>
<td>IV L</td>
<td>Recent surgery, no seizures</td>
<td>&lt;6</td>
<td></td>
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<tr>
<td>12</td>
<td>F/20</td>
<td>Nonlateralized Bi</td>
<td>HC</td>
<td>Bi L</td>
<td>Diffuse: L TL</td>
<td>IV</td>
<td>Not decided</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>F/29</td>
<td>L meso TL</td>
<td>L meso TL</td>
<td>L</td>
<td>Diffuse: L TL</td>
<td>IV L</td>
<td>Depth electrode study:</td>
<td>L regional onset</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>M/37</td>
<td>R meso TL</td>
<td>R HCS</td>
<td>Bi R</td>
<td>Diffuse: R TL</td>
<td>951 R</td>
<td>Recent surgery, no seizures</td>
<td>&lt;6</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>F/37</td>
<td>R meso TL</td>
<td>R HCS</td>
<td>B</td>
<td>Diffuse: R TL</td>
<td>951 R</td>
<td>1A</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>F/32</td>
<td>Bi independent L</td>
<td>HC atrophy</td>
<td>B</td>
<td>Complex: R &gt;L TL</td>
<td>IV</td>
<td>Not decided</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>F/30</td>
<td>R meso TL</td>
<td>B HCS</td>
<td>B</td>
<td>Diffuse: R TL</td>
<td>IV R</td>
<td>1A</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>F/34</td>
<td>L meso TL</td>
<td>L meso TL</td>
<td>L</td>
<td>None</td>
<td>IV L</td>
<td>Recent surgery, no seizures</td>
<td>&lt;6</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>M/44</td>
<td>L meso TL</td>
<td>B HCS</td>
<td>L</td>
<td>Diffuse: L TL</td>
<td>951</td>
<td>Not decided</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>F/39</td>
<td>R meso TL</td>
<td>R HCS</td>
<td>B</td>
<td>Diffuse: R TL</td>
<td>IV R</td>
<td>1A</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>F/19</td>
<td>L meso TL</td>
<td>L meso TL</td>
<td>L</td>
<td>Diffuse: L TL</td>
<td>IV L</td>
<td>3A</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>F/26</td>
<td>Nonlateralized B HCS, L&gt;R</td>
<td>B</td>
<td>Diffuse: L TL (slight)</td>
<td>951</td>
<td>Not decided</td>
<td>. . .</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>F/26</td>
<td>R meso TL</td>
<td>R HCS</td>
<td>B R</td>
<td>Diffuse: R TL</td>
<td>IV R</td>
<td>3A</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>M/19</td>
<td>L meso TL</td>
<td>L HCS</td>
<td>L</td>
<td>Diffuse: L TL</td>
<td>IV L</td>
<td>1A</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>F/28</td>
<td>R meso TL</td>
<td>R meso TL</td>
<td>R</td>
<td>None</td>
<td>IV R</td>
<td>1A</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>M/31</td>
<td>Nonlateralized L meso TL</td>
<td>L meso TL</td>
<td>L</td>
<td>Diffuse: L TL</td>
<td>IV</td>
<td>Not decided</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>M/53</td>
<td>L meso TL</td>
<td>L HCS</td>
<td>Bi L</td>
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<td>951 L</td>
<td>Scheduled for surgery</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>F/23</td>
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<td>Normal None</td>
<td>None</td>
<td>951</td>
<td>Not decided</td>
<td>. . .</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>F/37</td>
<td>L meso TL</td>
<td>L HCS</td>
<td>B</td>
<td>Diffuse: L TL</td>
<td>951 L</td>
<td>1A</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

Note.—Meso TL indicates focal mesotemporal lobe EEG location; FTL, regional frontotemporal EEG location; Bi, bilateral; HCS, hippocampal sclerosis; meso TS, mesotemporal lobe sclerosis, including hippocampus and surrounding areas, and IAP, intracarotid amytal procedure (Wada).

* See Table 1.
† FDG-PET hypometabolism categories modified from Henry et al (16).
‡ PET cameras were either an ECAT IV (IV) or an ECAT 951/31 (951).
§ Engel’s classification of postsurgical seizure outcome (38).
TABLE 3: PET versus MR spectroscopy in lateralization of temporal lobe epilepsy

<table>
<thead>
<tr>
<th>MR Spectroscopy*</th>
<th>PET Hypometabolism†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Lateral L or R</td>
<td>5 (0)</td>
</tr>
<tr>
<td>Bilateral L. or R</td>
<td>1 (0)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

* Categorization from Table 1.
† FDG-PET hypometabolism categories modified from Henry et al (16).
‡ This patient had bilateral temporal hypometabolism on PET scans, but worse on the side of the epileptic focus.

Discussion

The sampling location for the MR spectra and the regional abnormalities described on PET scans are not spatially identical. Most of the signal of the MR spectra in our study came from the deep temporal white matter, only a small fraction was from the hippocampus (3); on the other hand, most of the metabolic abnormalities seen on the PET scans were in cortical areas.

Since NAA is considered a neuronal marker, its signal in our spectra was produced by the NAA in the axons of the fibers in the deep white matter and partly by mesial gray matter structures (mainly the hippocampus). These axons originate in part from pyramidal cells of the temporal neocortex and the mesial structures (hippocampus and amygdala). Pathologic studies in patients with mesial temporal lobe epilepsy have shown that such abnormalities as neuronal loss and astrocitic reactions often extend beyond the hippocampus (24, 25). In one recent study (26), the most important FDG hypometabolism was reported to be in the hippocampus and the anterior temporal lobe, and it was attributed to neuronal loss. Other researchers have found a more pronounced glucose hypometabolism in the lateral temporal neocortex than in the mesial areas (12–14, 16, 19), and have conjectured that this is not always the result of a diminished number of neurons. The precise mechanism of this widespread hypometabolism is unclear, and different explanations have been proposed (27). Consequently, and because of its limited spatial resolution, PET is not capable of depicting the precise seizure focus; however, its reported sensitivity and specificity in depicting regional hypometabolism in the afflicted temporal lobe in patients with temporal lobe epilepsy are high (15).

Single-voxel proton MR spectroscopy gives an indication as to which is the side of epileptogenesis, because metabolites in standardized voxels are analyzed in both temporal lobes (3). Although there is a trend toward the use of chemical-shift imaging for the regional assessment of NAA in epilepsy (28–30) (Ende et al, “Quantitative...”; Duc et al, “Investigation...”), we were unable to perform this technique with the equipment used for the patients described here. One study compared PET with chemical-shift imaging in the cerebellar hemisphere. In a patient with cerebellar diaschisis, NAA was more abundant in the white matter than in the cortex (31). FDG hypometabolism in the cerebellar cortex was accompanied by a decrease in NAA, mainly in the white matter. Therefore, it is reasonable to assume that metabolic alterations seen in the spectra and the changes in glucose metabolism depicted by PET may be attributed to the same cells.

Our study shows more temporal lobes with abnormal NAA/(Cho+Cr) ratios than with FDG hypometabolism. In most of our patients, the imaging abnormalities were confined to the hippocampus (Table 2). Of 42 temporal lobes with low NAA/(Cho+Cr) ratios, only 25 showed hypometabolism on PET scans (Table 3), and all temporal lobes with hypometabolism at PET had an abnormally low NAA/(Cho+Cr) ratio. Furthermore, six patients had normal PET findings. Four of these patients had unilateral low NAA/(Cho+Cr), ipsilateral to the side predicted by EEG and MR imaging abnormalities, and one subject had bilateral low NAA/(Cho+Cr) ratios, but had concordant seizure lateralization by EEG and MR imaging on the asymmetry index. One last patient had no abnormalities on either PET scans or MR spectra. This indicates that a low NAA, depicted here as a low NAA/(Cho+Cr) (3, 32), is a more sensitive marker of neuronal dysfunction than is glucose hypometabolism depicted by PET. If we accept the hypothesis that the metabolite changes depicted on MR spectra and PET
scans are co-localized to the same cells, it is possible that the glucose hypometabolism represents a more advanced state of neuronal damage than does low NAA. Diminished NAA/(Cho + Cr) and glucose metabolism may be sequential and may result from neuronal exhaustion and microstructural or metabolic reorganization after prolonged epilepsy.

Repeated electrical stimulation can produce electrophysiologic, metabolic, and perhaps even morphological changes in local tissue (33). It is known that stimulus-produced seizure activity can be progressively intensified by repeated high-frequency stimulation of certain components of the limbic system at intervals ranging from minutes to days (34, 35). The mechanism underlying this “kindling” may be similar to long-term potentiation, in which brief periods of intense electrical activity give rise to a persistent change in synaptic activity.

It is then possible that the epileptic focus, of which the substrate often is hippocampal sclerosis, initiates a seizure. Electrical signals are propelled to connecting neurons locally and regionally, but in certain instances also to areas farther away and to the contralateral side. Neurotransmitter imbalances result first, and more advanced metabolic alterations, such as diminished glucose metabolism, build over years of epileptic activity. This leads to a weakening of the neurons and eventually to cell death and diminished neuronal cell counts. Coregistration of PET images and metabolic maps from chemical-shift imaging studies may provide an answer to this enigma, as local NAA concentration can be shown with this technique (28–30).

It has been shown that regional hypometabolism can recover in unresected areas after temporal lobectomy for temporal lobe epilepsy (36). This means that, to some extent, the changes in metabolism are reversible. Regional interictal hypometabolism in temporal lobe epilepsy can, in some cases, be accounted for by a diminished neuronal count, but it is clear that other factors related to epilepsy also contribute to metabolic dysfunction (27).

The exact mechanism of neuronal damage or dysfunction is unclear (27), as is the possible relationship between low NAA and glucose hypometabolism. Despite the fact that NAA is present in high concentrations within the brain, little is known about its role in normal function or disease states (37). Studies have suggested that NAA is largely but not exclusively present in neurons and that NAA is more abundant than aspartate (38, 39). Glutamate and aspartate meet many of the criteria for excitatory neurotransmitters, and are used by some of the most widely distributed neuronal types. The metabolism of glutamate, aspartate, and NAA is linked to the mitochondria. Both aspartate and glutamate are nonessential amino acids and are synthesized from glucose and other precursors (40). As a reaction to seizures in temporal lobe epilepsy, probable changes in aspartate and glutamate metabolism result in a lowering of the NAA pool in interconnecting neurons.

Glucose is also used as the main energy source for neurons. A diminished glucose uptake as depicted by PET is a reflection of a diminished glucose use rate in the tricarboxylic acid cycle of the neurons and a lower oxidation state, again a mitochondrial function. It is likely that the metabolic abnormalities depicted here by MR spectroscopy and PET are linked through mitochondrial dysfunction.

Conclusion

Our study indicates that single-voxel proton MR spectroscopy is more sensitive in depicting metabolic abnormalities than is FDG-PET, and, therefore, patients with a negative PET scan benefit from spectroscopic studies to help lateralize the seizure foci. The possible relationship between low glucose uptake and use as shown on PET scans and a low NAA level as seen at MR spectroscopy remains unclear.

References

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