Evidence for Cortical Dysfunction in Spasmodic Dysphonia: Regional Cerebral Blood Flow and Quantitative Electrophysiology

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Cortical function was evaluated in 26 subjects with spasmodic dysphonia. Quantitative topographic electrophysiologic mapping (QTE) was employed to provide quantitative analyses of EEG spectra and auditory and visual long-latency evoked potentials. Single-photon emission computed tomography (SPECT) of the cerebral transit of Xenon-133 was used to evaluate regional cerebral blood flow. Left hemispheric abnormalities in cortical function were found by both techniques in 10 subjects and by at least one technique in 18 subjects. Right hemispheric abnormalities were observed by both techniques in 8 subjects and by at least one technique in 18 subjects. Most patients with cortical dysfunction in one hemisphere had cortical dysfunction in the other, while only 4 subjects had unilateral lesions as found by one of the two techniques. Eight subjects were normal by all measurements. Underlying structural abnormalities were detected by magnetic resonance imaging in 5/24 subjects. However, functional abnormalities (SPECT or QTE) were not observed at sites of structural abnormalities. SPECT and QTE were significantly related in identification of left hemispheric dysfunction (p = .037) with a trend in the right hemisphere (p = .070), and a significant congruence of SPECT and QTE findings occurred in the left anterior cortical quadrant (p = .011). These findings indicate that dysfunction of cortical perfusion and/or cortical electrophysiology is associated with spasmodic dysphonia in the majority of subjects studied. © 1990 Academic Press, Inc.
INTRODUCTION

Spasmodic dysphonia (SD) is a disorder of unknown etiology (Schaefer & Freeman, 1987) characterized by a strained–strangled voice quality, intermittent breathy phonation, and voice stoppages. Central nervous system (CNS) contributions have been suspected, but are difficult to investigate (Aronson, 1980) due to lack of animal models and an inability to monitor dynamic CNS activity. Resolution of the latter problem may lie in recently developed technology, including quantitative topographic analysis of cortical electrophysiology (QTE) and tomographic measurement of regional cerebral blood flow (rCBF) (Pool, Freeman, & Finitzo, 1987; Finitzo & Pool, 1987; Devous et al., 1987). This paper provides preliminary data concerning the use of these techniques to evaluate cortical function in SD.

Research in our laboratories and others provides evidence of neurologic involvement in subjects with SD. Abnormalities have been reported in the auditory brainstem response (ABR) (Finitzo-Hieber et al., 1981; Hall & Jerger, 1976; Hall, 1981; Schaefer et al., 1983) and in vagoparasympathetic regulation of gastric acid secretion and cardiac rhythm (Feldman et al., 1984). CNS structural lesions have been observed primarily in subcortical white matter underlying frontal lobe by magnetic resonance imaging (MRI) in approximately 25% of SD subjects, although no consistent anatomic focus has been identified (Schaefer et al., 1985). Even though MRI-observable abnormalities of cortical structure are infrequent in SD subjects, cortical function has not been investigated and might be disrupted. We have employed topographic electrophysiologic mapping (QTE) as a quantitative measure of cerebral EEG and evoked potentials, and single-photon emission computed tomography (SPECT) to measure cerebral perfusion in SD subjects.

If there is focal neuronal dysfunction and if that dysfunction alters both perfusion and electrophysiology, then one should observe a focal congruence between these measures. In that context, two specific questions were addressed in this study: (1) Is there evidence of cortical dysfunction manifested as alterations in electrophysiology or cerebral perfusion? (2) Should such dysfunction exist, is there a congruence between sites of electrophysiologic and perfusion abnormalities?

METHODS

Subject Selection

Twenty six subjects were drawn prospectively from subjects participating in extensive studies of vocal motor control disorders conducted by the Dallas Center for Vocal Motor Control at The University of Texas at Dallas and The University of Texas Southwestern Medical Center at Dallas. Entry criteria for the overall study and medical examinations, assessments of phonatory behavior, and MRI examinations have previously been published (Feldman et al., 1984; Schaefer et al., 1985). Eight males and 18 females with a mean age
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of 46 ± 12 years were included in this study. Informed consent was obtained from all subjects in compliance with the rules of the Human Subject Use Committee of The University of Texas at Dallas and the Institutional Review Board of The University of Texas Southwestern Medical Center at Dallas. All data were collected within 5 days, and SPECT data were collected 24 hr following QTE data. Data analyses (SPECT, QTE, MRI) were conducted and interpreted independently and blinded to all other results.

Regional Cerebral Blood Flow

RCBF was measured quantitatively in three tomographic cross-sections using the Tomomatic 64 SPECT (Medimatic A/S, Copenhagen, Denmark) as described by Stokely et al. (1980). This tomograph consists of four detector arrays, each containing 16 NaI (Tl) scintillation crystals mounted in a hollow-square configuration that rotates about the subject's head at 6 rpm. Special focused collimators define three transverse tomographic sections with centers 4 cm apart. Xenon-133 was administered in an air/oxygen mixture (10 mCi/liter) by inhalation during the first minute of a 4-min wash-in/wash-out procedure. The subject breathes room air during the remaining 3 min of the study. During the tomographic measurement of the cerebral transit of Xenon-133, activity in the lung is monitored by a scintillation probe placed over the right upper quadrant of the subject's chest. This lung activity is assumed to be proportional to the arterial blood concentration of Xenon-133 arriving at the brain. Three tomographic cross-sections are generated by filtered back-projection with attenuation correction according to the method of Kay and Keyes (1975). RCBF is calculated according to the double-integral method (Kanno & Lassen, 1979; Celis, Goldman, Henrichsen, & Lassen, 1981; Smith et al., 1984). The lung curve is used as the input function to the Kanno-Lassen algorithm to compensate for delivery of tracer by inhalation rather than by direct injection into the internal carotid artery (Devous, Stokely, & Bonte, 1985). RCBF images are displayed in a 64 × 64 matrix employing a 16-shade scale adjusted to range from zero flow to maximum flow. Transverse resolution is 1.7 cm and axial resolution is 1.9 cm.

Subjects were positioned in the tomograph using a face-marking template so that cross sections were obtained 2, 6, and 10 cm above and parallel to the cantho-meatal line (CML). They were studied supine with eyes open and ears unplugged in a dimly lit room with background noise originating primarily from instrument cooling fans. Subjects breathed through a fitted mouthpiece while nostrils were occluded by a spring clamp. Approximately 2 min adaptation time was allowed prior to initiating the study. Each subject was asked to take a deep breath at the beginning of the study after which no further communication occurred. These procedures and values in normal subjects, reproducibility, intersubject variability, and asymmetries have been described in detail by Devous et al. (1987).

Electrocortical Topography

Cortical electrophysiology was measured using a Nicolet brain electrical activity mapper (BEAM, Nicolet Instrument Co.) as a tool for examining both EEG and evoked potential topography (Pool et al., 1987; Duffy, Burchfiel, & Lombroso, 1979; Duffy, 1982). EEG electrodes were placed at 25 sites over the scalp (including three extra cerebral monitors and two earlobe reference electrodes) according to the 10–20 International System. Data were amplified by standard EEG amplifiers and then digitized at a rate of 250 Hz per channel in epochs of 2-sec duration. Each 2-sec epoch was then visually inspected for artifacts (e.g., muscle or eye movement contamination). Only artifact-free epochs were subjected to spectral analysis using fast Fourier transformation (FFT), and at least 30 epochs were analyzed. This process produced amplitude–frequency curves from each electrode over a frequency range from 0.5 to 32 Hz in 0.5-Hz increments. The individual FFT curves from each 2-sec segment were arithmetically averaged at each electrode to produce a mean FFT.
Normative data for adults, stratified by age in decades, are contained in the resident database of the BEAM system (Duffy et al., 1979; Duffy, 1982). These data have been supplemented with screened normal controls from our laboratories. In-house controls were extensively evaluated for neurologic, audiometric, and radiographic (MRI) abnormalities. In addition to the mean FFT, the standard deviation of the FFT has also been determined. This database allows analysis of a subject's data in terms of the standard deviation difference from the normal mean at each frequency step and at each electrode. After data collection and processing, color topographic maps are generated representing amplitudes or standard deviations from normal means. The latter technique is referred to as significance probability mapping (SPM).

Cortical long-latency EP's were recorded using auditory and flash visual stimuli (Duffy et al., 1979). EP's were simultaneously recorded from each electrode used in the EEG analysis at a digitization rate of 25 Hz, resulting in dwell times of 4 msec. Both auditory and visual stimuli were delivered pseudorandomly between 1.25 and 1.75 sec per stimulus, and the response was signal averaged over a 512-msec poststimulus period. A 512-msec prestimulus baseline was also available to evaluate noise and adequacy of averaging. As above, age-dependent normative data and standard deviations are available for individual subject comparisons. As with EEG spectra, EP data were displayed as color maps representing amplitude, polarity, or standard deviation for each 4-sec latency measurement. Thus, 128 images were available for analysis for each 512 msec of poststimulus activity.

Data Analysis

Descriptive statistics included frequency distributions for categorical variables such as age, sex, and findings on SPECT and QTE. RCBF abnormalities in SD subjects were identified visually by experienced observers and were compared to similarly obtained findings in normal controls screened for any history of neurologic or psychiatric illness. Each observer had a visual interpretation experience of more than 3000 SPECT rCBF images at the time of this study. Abnormalities were defined as flow reductions below levels observed in healthy subjects evaluated in the prior experience of the observers. Further, observer reliability was subsequently evaluated by blinded readings of rCBF images in a mixed sample of patients and normal control subjects. The frequency of false-positive observations (interpreting an image as abnormal in a control subject) was taken as an index of reliability. Observer reproducibility was evaluated by comparing the result of the initial evaluation of this blinded data set to a second reading obtained 2 months later.

Electrophysiologic data were analyzed for either EEG spectra or EP amplitude abnormalities. A 3-Hz-wide EEG spectral band between 0.5 and 8 Hz (i.e., delta and theta frequency bands) must have had an average value greater than 3 standard deviations from that of the normative data base to be considered abnormal. Abnormalities in EP amplitudes were identified only when three separate occurrences of at least 12-msec duration, each greater than 3 standard deviations from the normal mean, were observed. Data were examined to assure such abnormalities were amplitude related and not due to artifact or subcortical latency prolongations.

The statistical analyses of quantitative electrophysiology must account for multiple measures and nonnormal distributions. Failure to control for these problems can produce excessive false-positive results (Oken & Chiappa, 1986; Kahn, Weiner, Brenner, & Coppola, 1988). The decision rules described above have been developed to correct for nonnormal distributions and multiple correlated measures. Monte-Carlo simulations conducted in our laboratory indicate that false-positive rates of less than 5% occur when these decision rules are employed.
**SPECT/QTE Comparisons**

Congruence of abnormal cortical findings on QTE and SPECT was evaluated using Fisher’s exact probability test (Zar, 1974). In the context of this paper, we consider findings to be related if we fail to demonstrate independence on a Fisher’s exact probability test. The SPECT tomographic cross section 6 cm above the CML was used to determine presence of anterior or posterior cortical abnormalities in either the left or right hemisphere. Anterior quadrants contained principally frontal gyri and the anterior inferior portion of the parietal lobe, while posterior quadrants contained primarily temporal and occipital gyri. Anatomic designations within these quadrants cannot be discerned from the rCBF images themselves but are taken from a careful examination of human cross-sectional anatomy obtained at the same level and angle (Matsui & Hirano, 1978).

For comparison purposes, QTE abnormalities were classified as left anterior (electrodes F7 and F3); left posterior (T5); right anterior (F4 and F8); and right posterior (T6). These electrode sites were used to define cortical quadrants in order to achieve maximum anatomic overlap between the two techniques. Further, FP1 and FP2 electrodes tend to have a higher incidence of artifact (eye movement) than other sites. Although eye-movement artifact was carefully eliminated during data reduction, these electrodes were not included in the analysis in a conservative effort to minimize false-positive findings. TP3 and TP4 are not routinely collected. O1 and O2 were not used in the analysis because rCBF data from this region are dominated by high flows induced by visual stimuli in eyes-open subjects. Hemispheric abnormalities identified by either technique included all recording sites, and thus hemispheric findings could be larger in number than the sum of quadrant findings. SPECT and QTE evaluations were conducted blinded to the results of the alternate measurement.

This analytical approach does not take full advantage of the anatomic specificity of either technique. However, current instrumentation for these two measures does not permit extensive anatomic overlap. Since the purpose of this investigation was to document cortical dysfunction, and specifically to determine if abnormalities of both perfusion and electrophysiology were concurrent, we focused on an analysis scheme that permitted maximum comparisons between the measures. This is illustrated for the left hemisphere in Fig. 1. The distribution of 10-20 electrode sites as measured by Homan, Herman, and Purdy (1987) using CT confirmation of electrode sites is compared to the cross sections used for SPECT. Electrodes used for QTE/SPECT comparisons are identified as above.

**RESULTS**

The 26 subjects under investigation included 8 males and 18 females 46 ± 12 years of age (mean ± standard deviation). SD type (adductor, abductor, or mixed) and severity for each subject are reported in Table 1. MRI and ABR were performed on 25 of the 26 subjects. MRI was abnormal in 5, principally represented by increased signal intensity lesions in subcortical white matter. While peri-ventricular white matter abnormalities (so-called UBOs, unidentified bright objects) are frequently seen in older subjects, the abnormalities observed in this younger SD subject population were distinct from UBOs and thought to be clearly representative of structural damage. ABR was abnormal in 4. There was no subject overlap between ABR and MRI abnormalities. In addition, there was no significant correlation among age, sex, vocal characteristics, etiology, and MRI or ABR findings. Similar results were reported by Schaefer.
Normal subjects demonstrated a nearly continuous ring of relatively high cortical gray matter flows with somewhat lower flows centrally. Scatter and partial volume effects inhibit clear differentiation of gray from white matter with this technique. Asymmetry is minimal in normal subjects with right hemispheric flow slightly higher than left (Devous et al., 1987). In some normal individuals the nearly continuous cortical ring of gray matter flow is broken, most commonly in the posterior temporal region and sometimes in the frontal regions, yielding a "Maltese cross" appearance (Devous et al., 1987, 1985). Since subjects were studied with their eyes open, high flows were frequently seen in the visual cortex.

False-positive rates evaluated in control subjects were low and varied with region. For the four regions evaluated in these normal control subjects, the false-positive rates were left anterior—13%; right anterior—3%; left posterior—10%; right posterior—10%. Observer reproducibility, derived from two interpretations of the same blinded data set separated by 2 months, was 93%. Pattern variations observed among normal individuals may be due partially to the use of an external anatomic reference for head positioning. Positioning in relation to the CML does not account for variations in head size. However, tomographic sections are
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### TABLE 1
**Patient Characteristics**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>SD type</th>
<th>Severity</th>
<th>MRI</th>
<th>ABR</th>
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<tr>
<td>1</td>
<td>AD</td>
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<td></td>
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<td>2</td>
<td>AD</td>
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<td>—</td>
<td>—</td>
</tr>
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<td>3</td>
<td>AB</td>
<td>Mild-moderate</td>
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<td>—</td>
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<td>Positive</td>
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<td>Positive</td>
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<tr>
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</tr>
<tr>
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</tr>
<tr>
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<td>10</td>
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<td>Moderate</td>
<td>—</td>
<td>—</td>
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<td>11</td>
<td>AD</td>
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<td>Positive</td>
<td>—</td>
</tr>
<tr>
<td>12</td>
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<td>Moderate</td>
<td>—</td>
<td>—</td>
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<tr>
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<td>—</td>
<td>—</td>
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<td>Positive</td>
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<td>—</td>
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</tr>
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<tr>
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<td>Positive</td>
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<tr>
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<td>Moderate</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>21</td>
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<td>Mild-moderate</td>
<td>—</td>
<td>—</td>
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<tr>
<td>22</td>
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<td>—</td>
<td>—</td>
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<tr>
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<td>Mild</td>
<td>—</td>
<td>—</td>
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<tr>
<td>24</td>
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<td>Moderate</td>
<td>—</td>
<td>—</td>
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<tr>
<td>25</td>
<td>Mixed</td>
<td>Mild</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>26</td>
<td>AB</td>
<td>Moderate</td>
<td>—</td>
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</table>

*Note. ND, not done; —, negative.*

The presence of rCBF abnormalities in SD subjects exceeded the false-positive rate observed in normal controls. Twelve of 26 SD subjects (46%) demonstrated abnormal left hemispheric rCBF at rest and 9 of these (35%) also had abnormal right hemispheric rCBF. Therefore, bilateral abnormalities were most common. No subject showed only right hemispheric lesions. The probability of such an occurrence is $p < .001$, assuming abnormalities are independently distributed (Fisher's exact test). On the basis of comparison to a human atlas (Matsui & Hirano, 1978), the most commonly involved anterior regions included the middle and superior frontal gyri and the cingulate (that is, the most anterior portions of the anterior quadrants). Posteriorly, the inferior and middle...
temporal gyri were most commonly involved (i.e., the middle portion of the posterior quadrants). Abnormalities for the SD subject group were distributed as follows: left anterior—35%; right anterior—23%; left posterior—27%; right posterior—27%.

**Cortical Electrophysiology**

Seventeen of 26 subjects (65%) had quantitative abnormalities either of EEG delta or theta spectral content, or auditory or visual evoked potential amplitude. Fifteen of these 17 were abnormal bilaterally, while 2 had only right hemispheric abnormalities. Thus, bilateral multifocal abnormalities were present in cortical electrophysiology data in a manner similar to that observed in SPECT rCBF measurements. Seven subjects had EEG spectral abnormalities. In 6 of these subjects, abnormalities were bilateral. Three of these 7 did not show concomitant EP amplitude deviations. Two of the 7 subjects demonstrated EEG spectral abnormalities that encompassed more than 14 electrodes. In fact, when they occurred, EEG spectral abnormalities tended to be widespread. Recall that only artifact-free spectral data were analyzed. Moreover, no changes could be attributed to drowsiness or medication as these subject variables were carefully controlled.

EP amplitude abnormalities were more common than those confined to EEG spectra. Fifteen subjects had abnormal studies based on auditory and visual evoked potential findings. These abnormalities were bilateral in 13/15. The two subjects with unilateral lesions manifested focal abnormality only over the right posterior quadrant (right posterior temporal/parietal cortex). The most frequent abnormal foci involved parieto-median frontal cortex (Fz, Cz), left temporal cortex (T3), and right posterior temporal cortex (T6).

In addition to quantitative EEG analysis, classical visual interpretation is always performed. Visual interpretation will differ from quantitative spectral analysis when there are intermittent or paroxysmal phenomena in the raw data as these are generally excluded from quantitative analysis. Thus, quantitative analysis does not replace visual inspection but is a complement to it. Visual inspection identified 12/26 abnormal records. Three of these 12 had normal quantitative EEG findings. Five of the abnormal records had diffuse delta or theta activity abnormalities. In four of the 5, quantitative spectral analysis confirmed the electroencephalographer’s visual interpretation. Three of the 12 abnormal records had nonspecific bursts of sharp activity. Only 1 of the 3 had quantitative spectral abnormalities and diffuse slow-wave activity on visual inspection. Four cases had focal intermittent left temporal slow activity. This intermittence precluded measurement of significant spectral abnormalities for all but one case. For that case, spectra also showed a slow focus over the left temporal cortex.
If classical EEG was also considered in defining sites of dysfunction, three additional cases had a left temporal focus. A total of 21 subjects can then be classified as abnormal on analyses of quantitative and classical EEG and EP.

**QTE/SPECT Relationships**

A synopsis of findings from all subjects is presented in Table 2. These data were used to analyze congruence between measures. Findings in the two techniques were related in the left hemisphere \((p = .037)\), and there was a trend for relationship in the right hemisphere \((p = .070)\). When abnormalities were subdivided into quadrants, the two techniques were related for the left anterior quadrant \((p = .011)\), with trends in the left \((p = .073)\) and right \((p = .045)\) posterior quadrants. Therefore, abnormalities in regional perfusion and electrophysiology were most congruent in the left anterior cortex.

Congruence between ABR or MRI and either QTE or SPECT was also evaluated using Fisher's exact test. No significant associations were observed. Brainstem pathology was associated with abnormalities in cortical electrophysiology in that 4/4 subjects with abnormal ABR had abnormal electrophysiology, but only 1/4 had abnormal SPECT. However, the small number of positive ABR findings precludes statistical evaluation. Five subjects had abnormal MRI, two of which were also abnormal on QTE, and only one of which was abnormal on SPECT.

**DISCUSSION**

The purpose of this investigation was threefold. First, we wished to discover whether there was cortical dysfunction in subjects with SD. There was substantial evidence to support a neurologic basis in most subjects, such as vagally mediated disturbances in gastric and cardiac function, and abnormalities in brainstem auditory pathways. It was a natural extension to ask whether or not the cortex was also involved.

<table>
<thead>
<tr>
<th>Left anterior</th>
<th>Right anterior</th>
<th>Left posterior</th>
<th>Right posterior</th>
<th>Left hemisphere</th>
<th>Right hemisphere</th>
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<td>7</td>
<td>3</td>
<td>5</td>
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<td>4</td>
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<td>SPECT only</td>
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<tr>
<td><strong>p</strong>*</td>
<td>.011</td>
<td>.248</td>
<td>.073</td>
<td>.045</td>
<td>.037</td>
</tr>
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</table>

* \(p\) value as determined by Fisher's Exact Probability Test for congruence of QTE and SPECT findings.
Our current data strongly support an involvement of the cortex in a significant number of subjects with SD based on abnormalities in cerebral perfusion and cortical electrophysiology.

Our second question was whether abnormalities in cortical function, if present, would have a focal pattern. The answer to this question may be unresolved. Both techniques demonstrated bilateral, multifocal abnormalities much more frequently than isolated unilateral lesions. While there was a congruence in the left anterior quadrant, possibly implicating a more common involvement of this region, the data do not support the concept that a single lesion in this site is sufficient to produce SD. We continue to investigate whether there is a pattern to multifocal lesions.

Finally, we wanted to know whether there was some relationship between cortical dysfunction as measured by cerebral perfusion and cortical electrophysiology. A strong relationship was found in the left anterior quadrant. In addition, these techniques had some hemispheric and posterior quadrant congruence, with little association in the right anterior quadrant. The findings may be influenced by the lack of direct anatomic overlap between the two techniques (Fig. 1). Further studies will be required to address this issue. The current data clearly indicate that cortical dysfunction, when present, leads to disturbances in both electrophysiology and perfusion within the same hemisphere. It is interesting to note that QTE abnormalities (65% of SD subjects) were more common than those found by SPECT (46%). The majority of electrophysiologic disturbances were seen in EPs, implying that some provocation may be required to uncover dysfunction. RCBF abnormalities might be more prevalent if observed following some form of stimulation.

It was also possible with these data to compare QTE or SPECT abnormalities with those observed by MRI or ABR. It is interesting that some association may exist between ABR abnormalities and QTE. These data should not be overinterpreted since only 4/26 subjects had abnormal ABR. However, all 4 had abnormal QTE while only 1/4 had abnormal SPECT. In contrast, QTE or SPECT abnormalities were not related to MRI findings. Five of the twenty-six subjects had abnormal MRI, and of these 2 were abnormal on QTE and 1 was abnormal on SPECT. No subjects with MRI abnormalities had abnormal ABR. Although no clear-cut structural basis for abnormalities observed by QTE and SPECT were found on MRI, it is noteworthy that MRI findings, when present, were more prominent in subcortical white matter underlying the left anterior cortical quadrant (Finitzo & Freeman, 1989). Since it has long been recognized that neuronal activity can be abnormal in the presence of intact structure, it is not surprising that we do not consistently associate structural (MRI) lesions with abnormalities of cortical function (Metter et al., 1983).
Both EEG and EPs have been employed to investigate disorders of vocal motor control (Hall, 1981; Hall & Jerger, 1976; Robe, Brumlik, & Moore, 1960). Information derived from EP studies had limited anatomic specificity because recordings were from single electrodes. Moreover, the subjective nature of classic EEG analysis has made validation difficult. Quantitative analytic techniques employed in our studies greatly facilitate data interpretation. The high frequency of abnormalities found in SD subjects by this technique may be a consequence of its improved sensitivity (Pool et al., 1987).

Measurements of regional cerebral perfusion have not been made previously in SD subjects. Speech and language function has been evaluated in normal individuals and in aphasics (Lassen, Ingvar, & Skinhoj, 1978), but disorders of vocal motor control such as SD or stuttering have not been investigated with this technology. This investigation is the first to explore cerebral perfusion or metabolism in disorders of vocal motor control. In this subject population, a high incidence of cortical dysfunction was observed.

While we have detected functional alterations in cortex, the complex integrative nature of brain does not permit unambiguous determination that the cortex is the site of primary pathology. Alterations at cortex could reflect functional diaschisis subsequent to abnormalities in brain regions with distant projections to the cortex. Specifically, Denny-Brown and Yanagisawa (1976) suggested that damage to basal ganglia or its cortical connections could disrupt the initiation and variability of movement and conceivably speech production. Similarly, studies during neurosurgical ablation procedures have shown that caudate stimulation causes speech arrest without interruption of verbal memory (Kwak et al., 1978). Motor speech abnormalities have been recorded in subjects with strokes involving principally the head of the caudate (Damasio et al., 1982). Further, Metter et al. (1983) identified functional metabolic lesions in the cortex of subjects with aphasia and subcortical structural lesions observed on CT scans. Unfortunately, the resolution of the currently employed SPECT system was insufficient to evaluate abnormalities in basal ganglia. Our observations of cortical dysfunction in SD patients may or may not be associated with concomitant subcortical dysfunction.

These lesion data suggest that injury to different portions of a system of neurons may produce a similar symptom complex. Further, in some settings involvement of combinations of sites may produce different symptoms than the sum of symptoms normally associated with involvement of each single site. In normal subjects Bartlett, Brown, Wolf, and Brodie (1987) found that homologous regions tended to covary during the phoneme stimulation. Further, they observed within hemisphere correlations of language centers to the left inferior frontal area (Broca's
area). Interhemispheric correlations were observed between Broca's area and frontal cortex in the left hemisphere and the homologous Wernicke's area in the right hemisphere. Their data suggest a bilateral organization for language comprehension. Thus, a concept of multifocal and bilateral functional abnormalities underlying disorders of speech is not unreasonable.

In summary, four significant findings emerge from this work. First, there are functional abnormalities in the cortex of subjects with SD. Thus, continuing evidence for a neurogenic basis for this disease is presented, and this evidence now extends to involve the cortex. Second, functional lesions present in one hemisphere were generally accompanied by abnormalities in the other in both measurements of perfusion and electrophysiology. Only 2/26 subjects showed unilateral QTE abnormalities, and 3/26 showed unilateral rCBF abnormalities. Therefore, the most common appearance of cortical dysfunction was multifocal and bilateral. Third, the occurrence of an abnormality within a hemisphere by one technique was associated with an abnormality in the same hemisphere by the other technique. This finding implies that these measures are sensitive to similar processes. It also provides validation for the existence of multifocal functional abnormalities. The fourth finding of importance is the congruence of these two measures in the left anterior quadrant despite minimal anatomic overlap. This suggests that the left anterior quadrant is more consistently involved than other brain regions in subjects with SD. Regional cerebral blood flow measurements and quantitative electrophysiologic mapping used in concert have enhanced inferences of focal neuronal dysfunction in SD.

REFERENCES


