Evaluation of brain function in severe human head trauma with multimodality evoked potentials

Part 2: Localization of brain dysfunction and correlation with posttraumatic neurological conditions

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Electrophysiological investigations were undertaken in 51 comatose patients with severe head trauma to locate areas of brain dysfunction and to relate the loci of dysfunction to the patient's posttraumatic neurological condition. On the basis of evoked potential data, the presence of decortication or decerebration depended on cerebral hemispheric dysfunction. Brain-stem dysfunction, defined by evoked potentials, did not correlate with posturing. On the other hand, impaired oculocephalic responses and bilateral abnormal pupillary light responses were associated with brain-stem dysfunction, while hemispheric dysfunction did not correlate with either. Duration of coma was dependent on hemispheric dysfunction. Brain-stem dysfunction was not significantly associated with prolonged coma. Furthermore, 80% of the head trauma patients who had Grade I or II multimodality evoked brain-injury potentials recorded in the acute period following head trauma (mean Day 3) became responsive within 30 days of their injury. Graded somatosensory brain injury potentials appeared to be a powerful prognostic tool as they significantly correlated with the patient's final outcome even when recorded early after injury. Abnormal multimodality evoked potentials recorded acutely consistently defined dysfunction of the visual, auditory, and motor systems in comatose patients, and were considerably more effective than the clinical neurological examination in diagnosing persisting focal deficits of these systems.

KEY WORDS • evoked potentials, multimodality • electrophysiology • head trauma, human • brain-stem dysfunction • cerebral hemisphere dysfunction • evoked brain-injury potentials

Improved methods of evaluating central nervous system function are needed in comatose patients with head trauma to better localize areas of brain dysfunction and to examine the relationships that exist between loci of neuronal dysfunction and neurological disease states in the early and late stages following injury.

Evoked potentials have been used to diagnose functional compromise of a single sen-
sory system in cerebrovascular disease, auditory diseases including acoustic neuromas, spinal cord disease, and visual disorders. Investigators applying evoked potentials in human head trauma have also confined themselves to a single modality rather than to a multimodality approach, thereby limiting the effective scope of this technique. The potential clinical value of evoked potentials, moreover, has recently been augmented by the development of non-invasive methods for recording evoked responses from the brain stem. However, in spite of the growing body of literature on its use in other neurological diseases, little work has been done to investigate the full value of evoked potentials in severe human head trauma.

In the study described here, we assessed the value in each patient of the combined performance of somatosensory, visual, auditory, and auditory brain-stem (far-field) responses, namely, multimodality evoked potentials (MEP), to increase our ability to localize areas of brain dysfunction and our knowledge of the neurophysiological basis of a patient's posttraumatic clinical status. We believed this approach could be of value because evoked potentials depend on neuronal vitality for their realization and may be able to detect dysfunction in specific sensory systems as well as areas of brain traversed by many neural systems, such as the cerebral hemispheres or brain stem.

In this report we describe our experience in localizing brain dysfunction with MEP's in 51 patients with head trauma who were unresponsive to verbal commands. Specifically, we directed our investigations: 1) to define the relationships that exist between areas of brain dysfunction, localized in vivo with evoked brain-injury potentials, and post-traumatic neurological conditions such as decortication and decerebration, impaired oculocephalic responses, and bilateral abnormal pupillary light responses, as well as the duration of coma, and the patient's outcome; and 2) to determine the accuracy with which MEP's can localize dysfunction in specific neural systems and therefore contribute, in the acute period following injury, to the diagnosis in comatose head-trauma patients of focal neurological deficits such as hemiparesis, deafness, and retrobulbar visual disorders.

Clinical Material and Methods

Methods to obtain and analyze MEP's in severe head-trauma patients have been detailed elsewhere. One MEP study included the recording in a single patient of somatosensory, visual, auditory, and auditory brain-stem (far-field) potentials. Electroretinograms, eighth nerve action potentials, and peripheral nerve action potentials were also done to verify the integrity of the respective peripheral receptors.

Patient Series

Fifty-one patients, 18 female and 33 male, who ranged in age from 4 to 65 years (mean age 26), were studied initially at the bedside in the neurosurgery intensive care unit. Forty-nine patients were admitted on the day of injury, and three patients were admitted the day after injury in transfer from other hospitals. In 82% of cases the initial study was performed within the first 9 days after injury. The mean time of initial study was the third day, and follow-up evoked potentials were obtained as long as 30 months after injury.

All patients in this study were unresponsive to verbal commands for at least 4 days, some for over 3 months, as a result of severe head trauma. A patient unresponsive to verbal commands was defined as one in whom no movement or spoken sound occurred in response to the verbal commands of an examining physician. Twenty-eight patients had closed head injuries requiring no surgery. Of the 23 patients who were operated on, six had gunshot wounds, four depressed skull fractures, and 13 space-occupying lesions with an intact skull. Each patient was managed according to a protocol described by Becker, et al., and at no time was the patient's treatment changed in any way because of the findings of an evoked potential study.

Clinical Parameters

A neurosurgeon or neurologist not directly involved with the evoked potential study but associated with the head-trauma program examined each patient on the day of admission and at all subsequent times according to protocol. A prospective study schedule for
correlation of data was established in which an evoked potential study, neurological examination, computerized axial tomogram (CT), and angiogram were done, when possible, on Day 1 and Day 5 post-injury. An evoked potential study, neurological examination, and CT were done on Day 14 and at 3 months. Subsequent evoked potential studies done at 6 months or longer post-injury were correlated with the neurological examination alone. Operative findings in 23 cases and postmortem results in four cases were also included.

Because of the difficulties of acute patient care, the above schedule could not be adhered to in all cases. Serial evoked potential studies, for example, were recorded only an average of 2.38 times per patient (122 somatosensory, visual, and auditory studies and 97 auditory brain-stem studies were obtained from 51 patients).

In view of the unresponsive condition of the patients, and the goal of correlating specific clinical parameters with evoked potentials, the neurological examination consisted of determining level of consciousness, presence or absence of decorticate or decerebrate posturing, abnormal oculocephalic responses, bilateral abnormal pupillary light responses, and focal motor and sensory deficits.

The patients' outcomes were classified according to the recommendations of Jennett and Bond into the following categories: good recovery = resumption of normal life; moderate disability = disabled but independent; severe disability = conscious but dependent; persistent vegetative state = prolonged unresponsiveness; death. A patient's outcome was determined at from 3 months to 30 months post-injury except in patients who died or had an excellent result before 3 months. In 32 patients the final result was determined between 1 and 2½ years following injury.

Electrophysiological Localization of Brain Dysfunction
Multimodality evoked potentials recorded from each head-trauma patient (the brain-injury potentials) were graded in increasing order of abnormality from I to IV. For analysis the injury potentials were combined into two categories for each modality: Grades I-II, and Grades III-IV. If there was a difference in the grade of an evoked injury potential between one side or the other the most normal grade was used to avoid skewed data resulting from focal deficits. This was not done, however, when single neural systems were being evaluated specifically to detect focal deficits. The two categories of injury potentials thus formed in each modality were correlated with the clinical parameters at two different time periods following head trauma, mean Day 3 and mean Day 14. As an indication of the degree of correlation of each modality with the clinical parameters the Pearson coefficient of contingency for two-way tables as modified by Cramér was calculated. This measure of contingency yields a score of 1 if there is perfect correlation and a score of 0 if there is no correlation.

Correlations were also made between evoked injury potentials and neuroanatomic lesions of known location defined by autopsy, angiography, CT, or intraoperatively.

Results
Correlation of MEP's with Clinical Parameters
Decortication and Decerebration. After excluding five patients who were flaccid and areflexic at the time of their evoked potential study, an association was made between the presence or absence of posturing in 46 patients and their graded MEP's recorded on mean Day 3 after injury. Twenty patients were noted to have either decorticate or decerebrate posturing on one or both sides during the recording, while 26 patients were not posturing when the evoked potentials were done.

There was a significant association (p < 0.01; Fisher's exact test) between the presence or absence of posturing and visual, somatosensory, and auditory brain-injury potentials. Auditory brain-stem injury potentials, on the other hand, did not significantly associate with posturing (Table 1). The degree of correlation of each modality was: visual, 0.56; somatosensory, 0.64; auditory, 0.55; auditory brain stem, 0.18 (Pearson coefficient of contingency). Thus, brain-stem dysfunction, defined electrophysiologically, may not be as important as cerebral hemispheric dysfunction in determining posturing in head-trauma patients (see Discussion).
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TABLE 1
Correlation of multimodality evoked potentials on mean Day 3 and posturing*

<table>
<thead>
<tr>
<th>Visual</th>
<th>Somatosensory</th>
<th>Auditory</th>
<th>Brain Stem</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>no posturing</td>
<td>23</td>
<td>3</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>posturing</td>
<td>4</td>
<td>16</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>totals</td>
<td>24</td>
<td>22</td>
<td>28</td>
<td>18</td>
</tr>
<tr>
<td>(p &lt; 0.01)</td>
<td>(p &lt; 0.01)</td>
<td>(p &lt; 0.01)</td>
<td>(p &gt; 0.10)</td>
<td>(p &gt; 0.01)</td>
</tr>
</tbody>
</table>

*Flaccid patients were excluded. Injury potential grade based on best response. p values based on Fisher's exact test for 2 × 2 table.

**Impaired Oculocephalic Responses and Bilateral Abnormal Pupillary Light Responses.** Impaired oculocephalic responses on one or both sides (isolated oculomotor paresis excluded) were noted in 19 of 51 head-trauma patients. A significant association was found between oculocephalic responses and somatosensory, auditory, and auditory brain-stem injury potentials (p < 0.05, p < 0.01, p < 0.01, respectively; Fisher's exact test). Visual evoked injury potentials did not significantly associate with oculocephalic responses (Table 2). The degree of correlation of each modality was: visual, 0.18; somatosensory, 0.38; auditory, 0.62; auditory brain stem, 0.57 (Pearson coefficient of contingency). The electrophysiological data suggested a stronger relationship between impaired oculocephalic responses and brain-stem dysfunction than with cerebral hemispheric dysfunction.

Bilateral abnormal pupillary light responses showed the same relationship with the injury potentials as did the oculocephalic responses, implicating brain-stem dysfunction rather than cerebral hemispheric dysfunction in their genesis (visual, p > 0.10; somatosensory, p < 0.05; auditory, p < 0.01; auditory brain stem, p < 0.01).

**Duration of Coma.** Forty-three of 51 patients (eight patients who died were not included) were studied with MEP's in the early phase following head trauma (mean Day 3) to associate the duration of coma with brain-injury potentials. All patients were unresponsive to verbal commands when studied electrophysiologically. Three periods of duration of coma, 1 to 7 days, 8 to 30 days, and over 30 days, were correlated with the brain-injury potentials. A patient was placed in one of the three duration of coma intervals if he became responsive to verbal commands within that time.

Visual, somatosensory, and auditory near-field evoked potentials correlated significantly with duration of coma (p < 0.05, p <

**TABLE 2**
Correlation of multimodality evoked potentials on mean Day 3 and impaired oculocephalic response*

<table>
<thead>
<tr>
<th>Visual</th>
<th>Somatosensory</th>
<th>Auditory</th>
<th>Brain Stem</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal oculocephalic response</td>
<td>16</td>
<td>16</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>impaired oculocephalic response</td>
<td>13</td>
<td>6</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>totals</td>
<td>29</td>
<td>22</td>
<td>31</td>
<td>20</td>
</tr>
<tr>
<td>(p &gt; 0.10)</td>
<td>(p &lt; 0.05)</td>
<td>(p &gt; 0.01)</td>
<td>(p &lt; 0.01)</td>
<td>(p &gt; 0.10)</td>
</tr>
</tbody>
</table>

*Flaccid patients were excluded. Injury potential grade based on best response. p value based on Fisher's exact test for 2 × 2 table.
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TABLE 3

Correlation of multimodality evoked potentials with duration of coma*

<table>
<thead>
<tr>
<th>Duration of Coma (days)</th>
<th>Visual I-II</th>
<th>III-IV</th>
<th>Somatosensory I-II</th>
<th>III-IV</th>
<th>Auditory I-II</th>
<th>III-IV</th>
<th>Brain Stem I-II</th>
<th>III-IV</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-7</td>
<td>9</td>
<td>3</td>
<td>11</td>
<td>1</td>
<td>10</td>
<td>2</td>
<td>10</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>8-30</td>
<td>13</td>
<td>4</td>
<td>15</td>
<td>2</td>
<td>14</td>
<td>3</td>
<td>13</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>&gt;30</td>
<td>5</td>
<td>9</td>
<td>4</td>
<td>10</td>
<td>6</td>
<td>8</td>
<td>9</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>totals</td>
<td>27</td>
<td>16</td>
<td>30</td>
<td>13</td>
<td>30</td>
<td>13</td>
<td>32</td>
<td>11</td>
<td>43</td>
</tr>
</tbody>
</table>

*p Mean time of study = Day 3. All patients were unresponsive when study was done. Patients who subsequently died were not included. Injury potential grade determined by best response. p value based on $\chi^2$ test of association.

0.005, $p < 0.05$, respectively; $\chi^2$ test of association for $2 \times 3$ contingency table, while auditory brain-stem (far-field) potentials did not (Table 3). The degree of correlation of each modality was: visual, 0.39; somatosensory, 0.62; auditory, 0.42; auditory brain stem, 0.17 (Pearson coefficient of contingency). A correlation could not be found, however, between the evoked potentials and duration of coma when the periods 1 to 7 days or 8 to 30 days were considered alone. The electrophysiological data suggested a stronger correlation between duration of stem dysfunction than with cerebral hemispheric dysfunction.

At least 80% of patients who had either Grade I or II visual, somatosensory, or auditory near-field injury potentials recorded within the first 9 days posttrauma (mean Day 3) became responsive within 30 days of their injury; specifically, visual evoked potentials 81% (95% confidence level (CL), 62% to 94% confidence interval (CI)); somatosensory evoked potentials 84% (95% CL, 66% to 95% CI); auditory evoked potentials 80% (95% CL, 61% to 92% CI).

Outcome. Multimodality evoked brain-injury potentials recorded early (mean Day 3), and later (mean Day 14) in the hospital course were associated with the outcome of 51 patients. Outcome categories were combined so that good recovery and moderate disability were considered in one group and severe disability, vegetative state, and death in the other. For the second of the two association periods only 45 patients remained alive, while all 51 patients were included in the analysis for the first time period.

In the first period studied the only evoked potential modality to be significantly associated with outcome was somatosensory ($p < 0.01$; Fisher's exact test). The degree of correlation of each modality was: visual, 0.14; somatosensory, 0.62; auditory, 0.17; auditory brain stem, 0.16 (Pearson coefficient of contingency). If somatosensory brain-injury potentials recorded in this acute period following head trauma were Grade I or II, 90% of the patients could be expected to have a good recovery or to be only moderately disabled when examined 3 months or longer after head trauma (95% CL, 74% to 97% CI) (Table 4).

By the second time period the somatosensory evoked brain-injury potentials were again associated significantly with outcome ($p < 0.001$); the association of auditory brain-stem injury potentials with outcome also became significant ($p < 0.05$) (Table 5). The degree of correlation of each modality was: visual, 0.14; somatosensory, 0.80; auditory, 0.27; auditory brain stem, 0.46 (Pearson coefficient of contingency).

Focal Deficits. Hemiparesis was diagnosed in 15 of 51 patients within the first 9 days after head injury and correlated with somatosensory evoked brain-injury potentials performed in that same time period. Somatosensory brain-injury potentials were again correlated with the presence or absence of hemiparesis in the same 15 patients 3 months or longer after head injury. At that time (3 months later) hemiparesis persisted in only nine of the original 15 patients while six had recovered completely (Table 6).

Of the 15 hemiparetic patients studied early, six had Grade I or II somatosensory injury potentials and nine had Grade III or IV potentials. All six patients with Grade I or II abnormalities recovered from their hemi-
TABLE 4
Correlation of multimodality evoked potentials and outcome in initial study*

<table>
<thead>
<tr>
<th>Category</th>
<th>Visual</th>
<th>Somatosensory</th>
<th>Auditory</th>
<th>Brain Stem</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I-II</td>
<td>I-II</td>
<td>I-I</td>
<td>I-II</td>
<td>I-II</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>good recovery or</td>
<td>21  8</td>
<td>28  3</td>
<td>24  9</td>
<td>27  11</td>
<td>34</td>
</tr>
<tr>
<td>severe disability</td>
<td>13  9</td>
<td>6  14</td>
<td>10  8</td>
<td>6  6</td>
<td>17</td>
</tr>
<tr>
<td>totals</td>
<td>29  22</td>
<td>31  20</td>
<td>33  18</td>
<td>38  13</td>
<td>51</td>
</tr>
</tbody>
</table>

*Mean time of study = Day 3. Injury potential grade determined by best response. p value based on Fisher's exact test for 2 × 2 table.

paresis by 3 months while the nine patients with Grade III or IV somatosensory injury potentials all remained hemiparetic 3 months later (p < 0.001; Fisher's exact test). In contrast, clinical neurological examination forecasted only 40% of the cases of persisting hemiparesis when done within the first 9 days after head trauma.

Retrobulbar visual dysfunction defined by careful neuroophthalmic examination at 3 months or longer after injury was present in 10 of 33 patients examined (18 patients died or could not be accurately evaluated). The presence or absence of this deficit was compared to visual evoked injury potentials done early in the hospital course (mean Day 3) when these patients were still comatose and the status of retrobulbar visual function could not be determined (Table 7).

There was a significant association of visual brain-injury potentials and the presence or absence of retrobulbar visual dysfunction in the 33 patients (p < 0.001; Fisher's exact test). At this time (mean Day 3), clinical evaluation of visual dysfunction was correct in 30% of cases (3/10) while the electrophysiological evaluation was correct in 90% (9/10).

Auditory dysfunction, defined by audiometric examinations 3 months or more after head trauma, was present in six of 33 patients examined (18 patients had died or could not be evaluated). The presence or absence of auditory dysfunction was compared to auditory evoked injury potentials done early when the patients were still comatose and the presence or absence of auditory dysfunction was clinically unknown (Table 8). There was a significant association of auditory brain injury potentials with the presence or absence of auditory dysfunction in the 33 patients (p < 0.001; Fisher's exact test). In the early

TABLE 5
Correlation of multimodality evoked potentials and outcome in serial study*

<table>
<thead>
<tr>
<th>Category</th>
<th>Visual</th>
<th>Somatosensory</th>
<th>Auditory</th>
<th>Brain Stem</th>
<th>No. of Cases†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I-II</td>
<td>I-II</td>
<td>I-I</td>
<td>I-II</td>
<td>I-II</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>good recovery or</td>
<td>22  8</td>
<td>28  1</td>
<td>22  6</td>
<td>27  6</td>
<td>31</td>
</tr>
<tr>
<td>severe disability</td>
<td>9   6</td>
<td>3  13</td>
<td>9   8</td>
<td>8  8</td>
<td>14</td>
</tr>
<tr>
<td>totals</td>
<td>30  15</td>
<td>29  16</td>
<td>28  17</td>
<td>33  12</td>
<td>45</td>
</tr>
</tbody>
</table>

†Death or lack of appropriate serial study excluded six patients.
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**TABLE 6**

Electrophysiological evaluation of hemiparesis in 33 patients*

<table>
<thead>
<tr>
<th>Hemiparesis</th>
<th>Somatosensory Evoked Potentials</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute (resolved)</td>
<td>I-II</td>
<td>6</td>
</tr>
<tr>
<td>hemiparesis</td>
<td>III-IV</td>
<td>0</td>
</tr>
<tr>
<td>residual (permanent)</td>
<td>I-II</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>III-IV</td>
<td>9</td>
</tr>
</tbody>
</table>

(*Mean study performed on Day 3. Outcome determined between 3 and 30 months.
†Based on Fisher's exact test for 2 × 2 table.

stage clinical evaluation of auditory dysfunction was correct in 17% of cases (1/6) while the electrophysiological evaluation was correct in 83% (5/6).

**Correlation of MEP's with Neuroanatomic Lesions of Known Location**

*Frontal Lobe Lesions.* It was not possible to correlate any of the evoked potential modalities with the seven known frontal lobe neuroanatomic lesions that were verified in our patients. Frontal lobe lesions were electrophysiologically silent because of the lack of a technically suitable sensory system with which to challenge the frontal lobes (Fig. 1).

**TABLE 7**

Electrophysiological evaluation of retrobulbar visual dysfunction in 33 patients*

<table>
<thead>
<tr>
<th>Visual Dysfunction</th>
<th>Visual Evoked Potentials</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>visual dysfunction</td>
<td>I-II</td>
<td>1</td>
</tr>
<tr>
<td>no visual dysfunction</td>
<td>III-IV</td>
<td>9</td>
</tr>
</tbody>
</table>

(*Mean study performed on Day 3. Outcome determined between 3 and 30 months.
†Based on Fisher's exact test for 2 × 2 table.

**TABLE 8**

Electrophysiological evaluation of auditory dysfunction in 33 patients*

<table>
<thead>
<tr>
<th>Deafness</th>
<th>Auditory Potentials</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>deafness</td>
<td>I-II</td>
<td>1</td>
</tr>
<tr>
<td>no deafness</td>
<td>III-IV</td>
<td>24</td>
</tr>
</tbody>
</table>

(*Mean study performed on Day 3. Outcome determined from 3 to 30 months.
†Based on Fisher's exact test for 2 × 2 table.

**Fig. 1.** Schematic view of sensory pathways involved in the generation of multimodality evoked potentials. The sensory input generating somatosensory and auditory evoked potentials traverses more caudal regions of brain stem than does sensory input for visual evoked potentials.
We examined the premise that a change in volume or density of frontal lobe brain occurring after head trauma secondary to conditions such as edema, or hematoma formation, could change the latency, waveform, or amplitude of evoked potentials generated elsewhere (such as in the parietal lobe, or temporal lobe) when recorded by electrodes on the frontal scalp. If the evoked potential generated in the occipital lobe, for example, could be altered by having to pass through damaged frontal lobe to reach the frontal scalp electrode, then this could be of diagnostic significance. This premise proved to be untenable as the frontal scalp electrodes faithfully reproduced the activity of both normal and abnormal evoked potentials wherever they were generated. For example, the severely abnormal Grade IV somatosensory injury potentials resulting from a badly contused and dysfunctioning left parietal lobe (diagnosed intraoperatively during the removal of a large left acute subdural hematoma) appeared similar postoperatively, whether recorded from the left parietal lobe or the left frontal lobe scalp, in spite of the fact that a generous left frontal lobectomy was done in this patient (Fig. 2). It was therefore not essential to employ frontal lobe scalp electrodes for recording MEP's in head-trauma patients since little information could be gained for purposes of localizing brain dysfunction.

Parietal Lobe Lesions. There were five known focal parietal lobe neuroanatomic lesions in our study. The somatosensory evoked injury potentials were the only evoked potentials capable of localizing these lesions. If the somatosensory brain-injury potentials recorded after a sensory challenge (median nerve depolarization) were Grade III or IV the patient usually had a more serious neuroanatomic lesion. Figure 2A illustrates the somatosensory injury potentials recorded...
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Postoperatively on Days 4, 23, and 113 in a comatose patient with a severely damaged left parietal lobe (confirmed at operation). As late as 113 days after head trauma, the injury potentials recorded from scalp overlying the severely damaged left parietal lobe were still extremely abnormal in contrast to the almost normal somatosensory potentials recorded from the right parietal lobe. Brain-stem injury potentials, Grade I (Fig. 2C), and the visual injury potentials, Grade II (Fig. 2B), were not useful in localizing this parietal lobe lesion.

Spread of evoked potentials from the hemispheric area in which they were generated to the opposite hemisphere appears to be by volume conduction and not by a secondary or slower system of conduction that should be able to produce evoked potentials when the primary sensory cortex is absent. For example, scalp electrodes overlying the primary sensory cortex of the left parietal lobe recorded Grade IV somatosensory injury potentials in response to right median nerve depolarization (Fig. 2D). Electrodes over the right, opposite, parietal lobe also recorded Grade IV somatosensory potentials in spite of the fact that the right parietal lobe responded well (Grade I) to left median nerve depolarization (Fig. 2A). Had there been a slow secondary pathway of conduction, one would have expected an evoked potential to be present on the right side. It was concluded that somatosensory evoked potentials can faithfullly reflect parietal lobe dysfunction.

Temporal Lobe Lesions. Eight patients had proven temporal lobe lesions. Localization of these neuroanatomic lesions was possible in seven of eight cases (87.5%) if both the auditory near-field and visual injury potentials were examined. Figure 3 displays the visual, auditory, and somatosensory brain-injury potentials, and postoperative CT scans in a patient who required a partial right temporal lobectomy. The CT scans (right) were performed postoperatively on the same day (see text).
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FIG. 4. Multimodality evoked potential study recorded in a patient with a suspected right thalamic mass. The patient’s angiogram had evidence of a mass effect in that the right lenticulostriate arteries were stretched and bowed laterally (*upper right*), while the left lenticulostriate arteries appeared normal (*lower right*) (see text).

patient who required a partial right temporal lobectomy for a hemorrhagic contused right temporal lobe. The CT scan demonstrated the postoperative changes secondary to the craniotomy and also a right ventricular catheter used to monitor the intracranial pressure. There were no further lesions demonstrated by the CT scan or found at surgery. The visual and auditory evoked responses (Fig. 3A and B) recorded from the right hemisphere were decreased in amplitude and the waveforms altered compared to the normal, left, hemispheric responses. Somatosensory potentials, on the other hand, were symmetrically Grade I, offering no help in localizing this focal lesion. Later in the hospital course when this patient became responsive she was found to have a left incongruous superior quadrantic hemianopsia. Based on correlations with the neuroanatomic data, it appeared that both visual and auditory evoked injury potentials were necessary for accurate localization of temporal lobe dysfunction.

**Occipital Lobe Lesions.** There were two known focal occipital lobe neuroanatomic lesions defined at surgery. The visual evoked injury potentials alone correlated well with these lesions as long as care was taken to perform electroretinograms to avoid confusion with retinal dysfunction (see Fig. 7 in Part 1 of this study).

**Diencephalic Lesions.** In two cases a neuroanatomic diencephalic lesion was suspected, both angiographically (Fig. 4 *right*) and because the symptoms of the syndrome of Déjerine-Roussy were present. These patients had normal visual evoked injury potentials and auditory brain-stem potentials with mildly abnormal auditory near-field potentials (Fig. 4B and C). The somatosensory evoked potentials related to the side of the lesion, however, were abnormal and the capacity to fatigue the system with repetitive trials was present (Fig. 4A) in both cases.

These two cases were unique in that we were not able to fatigue a neural system with
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**Brain-Stem Lesions.** Neuroanatomical brain-stem lesions were difficult to verify except at autopsy, and as a result only three confirmed cases were available with which to correlate MEP data.

The gross autopsy examination of one patient who died 10 days after head trauma revealed a cerebrum that was moderately edematous especially on the side of the partial left temporal lobectomy that had been done on the day of admission. The brain stem was grossly normal except for two small hemorrhages in the pons (Fig. 5). Microscopically, however, many small hemorrhages and clusters of microglial cells (del Rio Hortega silver carbonate stain) were seen to be scattered throughout the midbrain, pons, and medulla.

Somatosensory and auditory near-field brain-injury potentials were Grade IV in this patient and the auditory brain-stem potentials were Grade III (Fig. 6A, B, and D). A normal simultaneous eighth nerve action potential ruled out eighth nerve focal damage as a cause of the severely abnormal auditory responses (Fig. 6D). Visual injury potentials were bilaterally Grade I (Fig. 6C). Thus, the results of both modalities whose pathways traverse the medulla, pons, midbrain and part of the diencephalon, namely, somatosensory

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**Fig. 5.** Sections of the brain stem at autopsy revealed many small hemorrhages and clusters of microglial cells on the microscopic examination.

**Fig. 6.** Multimodality evoked potential study recorded in vivo in the same patient as shown in Fig. 5 (see text).
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FIG. 7. Multimodality evoked potential study recorded from a patient 6 hours before his death from right uncal herniation confirmed at autopsy (see text).

and auditory near- and far-field potentials, were severely abnormal. The visual evoked brain-injury potentials were unaffected by the brain-stem lesion probably because the sensory information evoking them did not traverse the damaged caudal regions of the brain stem (Fig. 1).

An MEP study was performed in another patient 6 hours before his precipitous death which was immediately preceded by the following clinical findings in order of occurrence: sudden dilatation of the right pupil, left hemiparesis, bilateral fixed and dilated pupils and bilateral decerebration, and flaccidity. Autopsy findings included right uncal herniation with brain-stem compression and hemorrhages.

The data recorded from this patient before the above sequence of events revealed Grade IV somatosensory brain-injury potentials recorded from right parietal scalp and Grade II somatosensory potentials recorded from left parietal scalp (Fig. 7A). This correlates well with right uncal herniation. Visual and auditory near-field injury potentials were Grade II (Fig. 7B and C) while the auditory brain-stem potentials were Grade I. Interestingly, at the time of the electrophysiological study, when uncal herniation had not yet become clinically apparent, a selective dysfunction of the right medial lemniscus (Grade IV right somatosensory evoked potentials) was observed. The auditory brain-stem potentials and lateral lemniscus were still Grade I (normal) at that time. It was concluded from the neuroanatomic correlations that in vivo localization of brain-stem dysfunction should be based on both brain-stem injury potential and somatosensory injury potential data.

Discussion

Recording of evoked potentials is a non-invasive electrophysiological means of intracranial penetration which depends on neuronal vitality for its realization and therefore offers advantages over other diagnostic techniques for the functional evaluation of areas of brain heretofore inaccessible in vivo. We have reported our preliminary investigations on the clinical applicability and prognostic value of evoked potentials in patients with severe head injuries as well as a method to analyze evoked potential data obtained from these patients so that the varied responses could be standardized and used effectively. For this report, 51 comatose patients with head trauma were studied to ascertain the relationship between foci of brain dysfunction, localized by MEP's, and several perplexing posttraumatic clinical states, such as coma, decortication, and decerebration, as well as clinical outcome. The scheme shown in Fig. 8 outlines our goal. Persisting focal deficits difficult to diagnose acutely by clinical neurological examination in unresponsive patients, such as deafness, visual dysfunction, and hemiparesis, were also evaluated electrophysiologically.
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AREAS OF BRAIN DYSFUNCTION

POST-TRAUMATIC NEUROLOGICAL CONDITION

Fig. 8. Scheme showing the relationship of evoked potentials and prognosis in patients with brain injury.

Dysfunction of Specific Neural Systems

The evaluation of dysfunction in specific neural systems with evoked potentials proved to be extremely valuable both in diagnosing focal deficits in comatose patients and in confirming the reliability with which electrophysiological data can localize specific areas of brain dysfunction. Visual and auditory evoked potentials recorded in comatose patients significantly correlated with retrolubar visual dysfunction and auditory dysfunction, especially from eighth nerve damage, and were more effective than the neurological examination in diagnosing dysfunction in these sensory systems early in the posttraumatic period. Because of the close topographical association of the somatosensory and motor systems, a comparison was made in the early posttraumatic period, and again at 3 months or later, between the presence or absence of hemiparesis and somatosensory evoked brain-injury potentials. Figure 9 right illustrates a Grade IV (absent) somatosensory injury potential recorded from the right parietal scalp in a patient with dense left hemiparesis. In patients with hemiparesis a Grade I or II somatosensory brain-injury potential indicated that a high degree of functional recovery could be anticipated; whereas, a Grade III or IV potential signified that hemiparesis would persist. This capacity to forecast functional recovery was not confined to somatosensory evoked potentials. A Grade III or IV brain-injury potential from any modality recorded early after head injury indicated severe brain dysfunction and predicted that functional recovery would not be seen in the patient after 3 months or more. Moreover, in correlating evoked potentials with autopsy and intraoperative findings, a Grade III or IV brain-injury potential was usually obtained only in the most severe neuroanatomical lesions.

Dysfunction of the Cerebral Hemispheres or Brain Stem

Location of dysfunction in brain regions in which many neural systems are present, such as cerebral hemispheres or brain stem, was accomplished by means of the wider scope afforded by MEP's, as opposed to one modality

Fig. 9. Brain images with the approximate location of sites of generation of multimodality evoked potentials superimposed. Left: The visual evoked potential is practically normal, while the somatosensory and auditory near- and far-field evoked potentials are absent in this comatose patient, suggesting brain-stem dysfunction. Right: The right parietal lobe response to left median nerve depolarization is absent in a patient with dense left hemiparesis. All other multimodality evoked potentials were almost normal in this patient.
alone, and correlating the electrical data with a topographical view of the sensory pathways. It is important to note that sensory input producing somatosensory and auditory near-field and far-field evoked potentials traverses regions of the medulla, pons, midbrain, and part of the diencephalon located caudal to the lateral geniculate body, the most caudal region traversed by sensory input producing visual evoked potentials (Fig. 1). Visual sensation leaves its caudal position in the lateral geniculate body and turns rostrally into the cerebrum passing through the temporal and parietal lobes into the occipital lobe. We suggest, therefore, that abnormal somatosensory and auditory near- and far-field (brainstem) evoked potentials recorded from comatose head-trauma patients with normal visual evoked potentials (Figs. 6 and 9 left) implicate dysfunctional brain stem more than dysfunctional cerebral hemispheres. On the other hand, an electrophysiological cerebral hemispheric dysfunction may exist if the data indicate normal auditory brain-stem (far-field) potentials and abnormal auditory near-field evoked potentials coupled with abnormal visual and somatosensory potentials.

Two lines of evidence in our results indicate that evoked brain-injury potentials as we have categorized them are capable of correctly localizing areas of brain dysfunction. The functional evidence indicates a significant association in each modality between abnormal evoked potentials and dysfunction of the appropriate specific sensory system as well as among several evoked potential modalities and dysfunction of areas of brain encompassing more than one sensory system. The neuroanatomical evidence indicates positive correlation between the location of dysfunctional brain in vivo by the evoked potential data and the location of neuroanatomical lesions at autopsy or operation.

Our results suggest that brain-stem dysfunction may not be as important as cerebral hemispheric dysfunction in determining decortication or decerebration after head trauma. On the other hand, both impaired oculocephalic responses and bilateral abnormal pupillary light responses were correlated with brain-stem dysfunction and not hemispheric dysfunction. Duration of coma following head injury was found, electrophysiologically, to be dependent on cerebral hemispheric dysfunction while brain-stem dysfunction did not correlate with prolonged coma. Furthermore, patients in whom either Grade I or II visual, somatosensory, or auditory near-field injury potentials were obtained within the first 9 days following injury became responsive within 30 days in over 80% of cases. Each patient's outcome, as defined above, was also correlated with the brain-injury potentials to determine if a specific result category could be predicted by one or more evoked potential modalities done early in the patient's hospital course. In patients whose somatosensory brain-injury potentials performed in the first week following trauma were Grade I or II, 90% could be expected to have a good recovery or to be only moderately disabled 3 months or more after head trauma. By the second time period studied (mean Day 14) brain-stem injury potentials could also be significantly correlated with outcome. Graded somatosensory evoked injury potentials appear to be powerful prognostic tools for evaluating outcome in the early period following head injury.

The oft-repeated assertion that patients who are decerebrate or who have prolonged coma following head injury yet do not have an intracranial mass lesion are suffering from primary brain-stem damage has been challenged by Strich,20,21 Oppenheimer,17 and more recently by Mitchell and Adams.15 The latter authors were unable to identify isolated brain-stem damage at autopsy in 18 patients in whom histological evidence of increased intracranial pressure was absent. They suggest, moreover, "... that the principal reason for the difficulty in defining primary localized brain stem damage due to blunt head injury is that it does not exist as a pathological entity." The so-called clinical syndrome of primary brain-stem damage "... may equally easily result from a lesion above the brain stem..." The evoked potential data presented in this report show a high degree of correlation between decortication, decerebration, prolonged coma, and hemispheric dysfunction rather than brain-stem dysfunction, and may well be an in vivo physiological confirmation of this aspect of head-injury pathology.

Improved patient care does not, in the last analysis, depend on any single measure. Thus, the full value of an electrophysiological assessment of brain function cannot be realized without the many other bits of information processed by the physician. Multi-
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modality evoked potentials do, however, add another dimension to the evaluation of the patient with head trauma because they offer the opportunity to penetrate the brain non-invasively and examine the functional integrity of neural systems.

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References

5. Feinsod M, Auerbach E: Electrophysiological examinations of the visual system in the acute phase after head injury. Eur Neurol 9:56-64, 1973

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