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Factors Affecting Successful Localization of the Central Sulcus Using the Somatosensory Evoked Potential Phase Reversal Technique

BACKGROUND: Perirolandic surgery is associated with an increased risk of postoperative neurological deficit that can be reduced by accurate recognition of the location of sensorimotor cortex. The median somatosensory evoked potential (MSSEP) phase reversal technique (PRT) reliably identifies the central sulcus (CS) intraoperatively, but does require additional surgical time. Awareness of factors that lengthen the time required for MSSEP PRT has important implications for surgical planning.

OBJECTIVE: To identify factors that affect the time required for CS localization via MSSEP PRT.

METHODS: Multivariate Cox regression analysis, applied in 100 consecutive cases of perirolandic surgery at a single institution from 2005 to 2010, during which CS localization was attempted via a standardized MSSEP PRT.

RESULTS: The CS was reliably identified in 77 cases. The mean time to identification was 5 minutes (SD = 5; range, 1-20 minutes). Lesion location either very close to the CS (within the postcentral gyrus) or at an intermediate distance (with edema extending very close to the CS) independently decreased the rate at which the CS was identified by 73% (hazard ratio: 0.27, P < .001) and 55% (hazard ratio: 0.45, P = .007), respectively. Highly destructive pathology reduced this rate by 42% (hazard ratio: 0.58, P = .03), after adjusting for other important factors. Epidural recording, age, and the presence of a burst suppression pattern on the electroencephalogram had no effect.

CONCLUSION: MSSEP PRT is an effective method for CS identification and only marginally lengthens the operative time. However, difficulty in CS localization can be expected in the presence of postcentral gyrus lesions, edema distorting perirolandic anatomy, and with highly destructive pathology.

KEY WORDS: Brain neoplasms, Cerebral cortex, Electrophysiology, Intraoperative, Monitoring, Neurosurgery, Somatosensory evoked potentials

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S urgical procedures in the perirolandic region require accurate identification of the central sulcus (CS) to minimize the risk of inadvertent injury to the sensorimotor system. Studying the cortical anatomy on preoperative imaging is often a useful first step, as there are many recognized patterns of the frontal sulci useful in identifying the CS.¹ The superior frontal sulcus terminates posteriorly in the precentral sulcus, which is imme-

ABBREVIATIONS: CI, confidence interval; CS, central sulcus; ECoG, electrocorticogram; HR, hazard ratio; MSSEP, median somatosensory evoked potential; PRT, phase reversal technique diately anterior to the CS.² On a paramedian sagittal view, the CS may be identified as the notch just anterior to the termination of the marginal branch of the cingulate sulcus.³ Also, the CS forms the posterior border of the omega-shaped knob classically recognized as the hand motor region in the axial plane.⁴ Furthermore, on high-resolution T2-weighted magnetic resonance imaging (MRI), cortical thickness can be a helpful indicator, as the anterior (motor) bank of the CS is approximately twice as thick as the posterior (sensory) bank.⁵ In addition to these anatomic landmarks, functional imaging studies such as magnetoencephalography and functional MRI can be used to identify the location of the CS.^{6,7}

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828 | VOLUME 72 | NUMBER 5 | MAY 2013

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For a variety of reasons, however, preoperative studies are often insufficient to accurately identify the CS. The presence of mass lesions can distort the gyral and sulcal anatomy, making standard anatomic landmarks difficult to interpret.⁸ Slow-growing lesions may even lead to functional reorganization, rendering anatomic inferences incorrect. Therefore, although preoperative imaging studies can be useful adjuncts in CS identification, intraoperative identification of the CS with neurophysiological recordings remains the gold standard.⁹⁻¹¹

Intraoperative CS identification can be accomplished effectively by the median somatosensory evoked potential (MSSEP) phase reversal technique (PRT), first described by Goldring¹² and Gregorie and Goldring.¹³ The CS is readily identified by the phase reversal of the approximately 20-ms latency somatosensory evoked potential elicited by median nerve stimulation. Whereas this method provides the neurosurgeon with reliable intraoperative information, it does increase surgical time. An understanding of the impact that various patient- and lesionrelated variables have on the time required for CS identification can assist in deciding whether to attempt CS identification with the PRT, as well as in providing an estimate of the time required. We therefore analyzed factors that may affect the success and time requirement for CS localization with MSSEP PRT.

PATIENTS AND METHODS

After institutional review board approval (protocol assurance number 2007P-002376), we retrospectively identified 257 consecutive cases of neurophysiological functional mapping performed during the period

2005 to 2010 at a single, quaternary level care center. One hundred cases met inclusion criteria and were included in this study.

Inclusion Criteria and Mapping Protocol

We included only cases in which MSSEP PRT was used intraoperatively to identify the CS as an initial neurophysiological mapping method (ie, before mapping via direct cortical stimulation) and regardless of its success. We excluded cases in which the intraoperative MSSEP PRT followed a similar procedure performed preoperatively via an implanted subdural electrode grid in the video-electroencephalogram epilepsy monitoring unit.

All selected mapping cases were performed using a standardized MSSEP PRT protocol. The contralateral (to the operated hemisphere) median nerve was stimulated transcutaneously at the wrist by 2 disposable surface electrodes with repetitive electrical pulses at 3.17 Hz, 0.3-ms pulse width, and stimulus amplitudes between 10 and 25 mA. In each case, the smallest intensity that produced a good thumb twitch was used.

Averaged evoked cortical MSSEPs were recorded directly from the cortex via an 8-contact strip electrode (Ad-Tech Medical Instrument Corporation, Racine, Wisconsin). The strip was positioned so that it crossed and was perpendicular to the presumed direction and location of the CS at the level of the hand region on the lateral hemispheric convexity. Informative results were defined as obtaining a phase reversal (identified as a sharp change in polarity) and/or a sudden change in the morphology of the recorded MSSEPs, both of which reliably identify the location of the CS.¹⁴ The CS was thus identified as the sulcus located between 2 adjacent contacts that showed opposite polarities and/or different morphologies (Figure 1). The success of PRT was further confirmed by electrical cortical stimulation. Whether successful identifying motor cortex (direct stimulation-based motor mapping) will be the subject of future study.

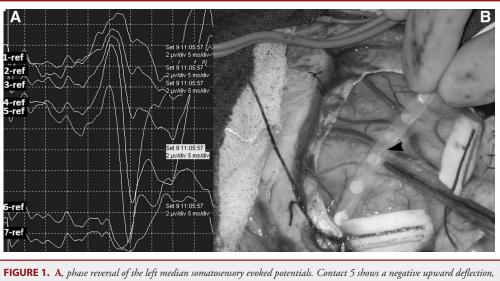


FIGURE 1. A, phase reversal of the left median somatosensory evoked potentials. Contact 5 shows a negative upward deflection, whereas contact 6 shows a positive downward deflection. According to the dipole orientation of median nerve cortical potentials, from the electronegatively charged somatosensory cortex toward to electropositively charged frontal regions, contacts 6 and 5 are respectively situated anterior and posterior to the central sulcus. **B**, exposed cortex showing the 8-contact recording strip. Contact 5 (indicated by the forceps) is posterior to the central sulcus (arrowhead), and contact 6 is anterior. Orientation: top is anterior, right is medial.

NEUROSURGERY

VOLUME 72 | NUMBER 5 | MAY 2013 | 829

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Both bipolar and referential montages were used, with each of the 8 contacts referenced to an electrode placed on the contralateral mastoid. Recording parameters included sensitivity 1 μ V/division and time base 5 ms/division; filter settings were low-frequency filter 30 Hz and high-frequency filter 500 Hz. We routinely use a relatively low high-frequency filter. We are aware that while this setting decreases the higher frequency artifact (eg, muscle artifact), and thus improves the recordings, it may also preclude identification of the faster frequency, smaller evoked potentials usually seen on the upward slope of N20, which are thought to be specific to the somatosensory cortex.¹⁵ All cases of significant pulsation or electrical artifact that precluded a reliable signal-to-noise ratio of the recording were excluded. In addition, we excluded cases in which appropriate stimulation of the median nerve was not confirmed by a good thumb twitch (eg, wrist edema, significant peripheral neuropathy or peripheral neuropathe).

In most cases in which an informative result was not obtained, the recording strip was repositioned (ie, translated or rotated). The recording was then repeated with the strip in the new position. For example, if all contacts recorded only negative peaks, we assumed that the strip was likely situated entirely posterior to the CS; thus, the strip was translated anteriorly in an attempt to cross the CS. The decision to stop mapping without having identified the CS was made in conjunction with the neurosurgeon, neurophysiologist, and anesthesiologist. This decision was made after considering several factors, including the amount of time already spent mapping, the anticipated length of the remainder of the surgical procedure, the physiological state of the patient, the estimated likelihood from existing data that the planned surgical procedure would encroach on sensorimotor cortex, and difficulties already encountered from the perspective of the surgeon, neurophysiologist, or anesthesiologist. To avoid having to reposition the recording strip, some have advocated the use of a subdural grid of electrodes rather than a single strip.¹⁶ We do not routinely use grids for CS identification at our institution, however, because of the fact that placement of such a grid requires larger craniotomies and more time to optimize the contacts with the cortical surface of a larger number of recording electrodes.

Starting half an hour before initiation of recordings and until the end of the mapping procedure, general anesthesia was maintained solely with propofol and an opiate infusion (total intravenous anesthesia).¹⁷ No inhalational anesthetic agents were used during MSSEP PRT.

Data Collection

For each case, we identified the following variables for analysis:

- Results of MSSEP PRT (dichotomous outcome variable). Unsuccessful cases were those in which the results were not informative and thus the CS could not be reliably identified. Successful cases were those in which the CS could be reliably identified based on the results of the neurophysiological recordings.
- 2. Lesion location (predictor variable classified in 3 categories). Based on anatomic landmarks previously described in literature,^{17,18} we measured the distance from the edge of the lesion or perilesional edema margin to the CS, as identified on preoperative 1.5-T MRI. According to this distance, we classified the patients into 3 groups. Group 1 (far) included cases with either frontal or parietal lesions in which the lesion and edema margins were more than 5 mm from the CS and therefore not causing significant mass effect on the perirolandic region. Group 2 (intermediate) included frontal or parietal lesions more than 5 mm from the CS, but with edema extending 5 mm or less from the CS. These lesions could therefore

have exerted mass effect and anatomic distortion of the perirolandic region. Group 3 (near) included lesions situated in close proximity to the somatosensory cortex, defined as postcentral gyrus lesions 5 mm or less from the CS. These lesions could therefore have additionally altered local physiology or function because of infiltration of neoplastic or necrotic tissue into the postcentral gyrus.

- 3. Pathology (dichotomous predictor variable). Pathology was classified as either less destructive (group 1) including low-grade gliomas (WHO grades I and II), brain metastases, and neurodevelopmental lesions or highly destructive (group 2) including high-grade gliomas (WHO grades III and IV) and non-neoplastic invasive pathology.
- 4. Age (dichotomous predictor variable). Patients were classified as either younger than 50 years of age (group 1) or older than 50 years of age (group 2).
- 5. Degree of cortical suppression (dichotomous predictor variable). The electrocorticogram (ECoG) was classified as containing either a continuous background (group 1) or the presence of a burst suppression pattern (group 2). ECoG was performed using the same 8-contact subdural strip electrode initially used for MSSEP recordings.
- 6. Location of the MSSEP recordings (dichotomous predictor variable). Recording location was classified according to the location of the electrode in relation to the dura, either subdural (group 1) or epidural (group 2).

MRI data, pathology results, anesthesia details, and demographic reports were acquired from the electronic medical records. The results of the MSSEP PRT technique, as described in formal reports, were compared with the results from the reanalysis of raw neurophysiological data by a neurophysiologist blinded to the other identified variables. Only cases in which these 2 sets of results were concordant were included in the study. Intraoperative navigation was used in all procedures and therefore not included in the model.

Statistical Analysis

We performed univariate and multivariate analyses of the predictive capacity of the variables listed on the time needed to identify the CS with MSSEP PRT using a linear Cox regression analysis (SAS software, version 9.1; SAS Institute, Cary, North Carolina). Results are therefore expressed as hazard ratios (HRs) with 5% to 95% confidence intervals (CIs). All variables were categorical, with age, degree of cortical suppression, location of the recording, and pathology each as 2-category variables, and lesion location as a 3-category variable, as described previously. Group 1 categories were considered as reference for all the variables. Significance was predefined at P < .05.

RESULTS

One hundred consecutive patients undergoing the same number of craniotomies fulfilled the inclusion criteria for our study and were included in the analysis. Using the MSSEP PRT, the CS was successfully localized in 77 patients. Among these, the mean time to identification was 5 minutes (SD = 5; range, 1-20). In 20 cases, informative recordings were obtained within 1 minute.

There were 53 right-sided and 47 left-sided craniotomies. The age range was 7 to 78 years, with a mean of 50 years. Sixty-eight lesions were exclusively confined to the frontal lobe, 23 lesions

830 | VOLUME 72 | NUMBER 5 | MAY 2013

www.neurosurgery-online.com

were parietal, and 9 were frontoparietal. The lesions and perilesional edema were far from the perirolandic region in 45 cases, at an intermediate distance in 36, and near the perirolandic region in 19. The average time spent to identify the CS was 3 minutes for the far group, 5 minutes for the intermediate group, and 7 minutes for the near group. In 7 cases, more than 10 minutes were spent identifying the CS: 4 of these were in the intermediate group and 3 were in the near group.

In 7 cases, no definite pathology was identified. In the less destructive group, there were 13 cases of neurodevelopmental lesions, 19 of brain metastases, and 15 of low-grade glioma (WHO grade I or II). In the highly destructive group, there were 39 cases of high-grade glioma (WHO grade III or IV) and 7 of invasive non-neoplastic pathology (1 of postradiation necrosis and gliosis, 5 of gliosis and/or cystic necrosis causing epilepsy, and 1 of multiple deep infarcts). Fifty patients were older than 50 years of age. Subdural recordings were conducted in 91 cases. Seventy-two of the 100 patients showed burst suppression on the ECoG. Table 1 summarizes the descriptive statistics and demographic data in our sample.

Univariate analysis (Table 2) demonstrated that proximity of the lesion to the putative location of somatosensory cortex was

TABLE 1. Patient Characteristics and Demographic Data					
Variable	No.				
Age, y					
>50	50				
≤50	50				
Sex					
Male	52				
Female	48				
Hemisphere					
Right	53				
Left	47				
Pathology					
Low-grade gliomas (WHO grades I and II)	15				
Brain metastasis	19				
Neurodevelopmental	13				
High-grade gliomas (WHO grades III and IV)	39				
Non-neoplastic invasive	7				
No definite	7				
Lobe					
Frontal	68				
Parietal	23				
Frontoparietal	9				
Location of the lesion in relation to somatosensory cortex					
Near	19				
Intermediate	36				
Far	45				
Deep cortical suppression					
Yes	72				
No	28				
Position of recording electrodes					
Epidural	9				
Subdural	91				

a significant predictor of increased time to CS mapping (P < .001 for the near category, P = .003 for the intermediate category). Destructive pathology also increased the time for successful mapping (P = .03). Epidural recording location, deep cortical suppression (as measured by the presence of a burst suppression pattern on the ECoG), and age were not significant predictors.

The multivariate analysis (Table 2) confirmed the same predictors that decrease the likelihood of successful CS localization:

- 1. A parietal lesion in close proximity to the somatosensory cortex (near group) independently reduces the rate of CS identification by 73% (HR: 0.27, 95% CI: 0.13-0.58, P < .001) (Figure 2).
- 2. A frontal or parietal lesion exerting mass effect on perirolandic anatomy because of an intermediate distance from the CS (intermediate group) independently reduces the CS identification rate by 55% (HR: 0.45, 95% CI: 0.25-0.81, P = .007) (Figure 2).

3. Highly destructive pathology independently reduces the rate by 42% (HR: 0.58, 95% CI: 0.35-0.96, P = .03) (Figure 3). Graphic representations of the results of this regression analysis can be found in Figures 2 and 3 in the form of survival curves. Age, degree of cortical suppression, and the location of the recording strip did not significantly alter the CS identification rate.

DISCUSSION

Perirolandic lesions must be approached with an accurate appreciation of the individual patient's functional anatomy to perform a safe and effective resection. New, severe postoperative neurological deficits can occur in as many as one fourth of patients undergoing resective surgery in this area, underscoring the need for diligence in identifying and preserving eloquent brain.^{10,19} Thus, pre- and intraoperative functional mapping of eloquent regions is of utmost importance in this type of surgery.

Several neurophysiological modalities for intraoperative assessment of functional-anatomic relationships exist and are routinely applied in either a simultaneous or stepwise manner depending on intraoperative findings and a variety of patient-centered factors.¹¹ As opposed to preoperative functional imaging techniques, the results of intraoperative neurophysiological mapping are not affected by brain shift and thus allow a more precise assessment of such functional-anatomic relationships.

Furthermore, neurophysiological techniques can be particularly useful in cases of functional reorganization of the cortex caused by the chronic presence of tumors (especially low grade), vascular malformations, or congenital lesions.²⁰⁻²³ In such cases, reliance on preoperative anatomic and functional imaging alone can be dangerously misleading, and intraoperative neurophysiological techniques are particularly useful. Furthermore, compared with other intraoperative neurophysiological mapping methods such as direct motor mapping, MSSEP PRT does not have the potential to trigger electroclinical seizures.

NEUROSURGERY

VOLUME 72 | NUMBER 5 | MAY 2013 | 831

Variables	Univariate			Multivariate		
	HR	95% CI	P Value	HR	95% CI	P Value
Lesion location						
Near	0.31	0.15-0.60	<.001	0.27	0.13-0.58	<.001
Intermediate	0.45	0.27-0.77	.003	0.45	0.25-0.81	.007
Destructive pathology	0.60	0.37-0.95	.03	0.58	0.35-0.96	.03
Epidural recording	1.52	0.69-3.36	.30	0.80	0.34-1.86	.60
Deep cortical suppression	1.34	0.78-2.30	.29	1.07	0.60-1.89	.82
Age $>$ 50 y	1.03	0.65-1.61	.91	1.40	0.86-2.27	.18

However, with each additional intraoperative testing modality that is used, operative time lengthens. The likelihood of any 1 technique providing sufficient diagnostic information should thus be known a priori to allow better surgical planning and anesthesia management. Although information presented in this study highlights the high likelihood of MSSEP PRT to identify the CS in a relatively short period of time (~1 minute in 20 of 77 cases of successful localization), it also identifies certain factors that could potentially slow down this process.

Cortical lesions can cause significant deviation from the expected location of eloquent cortex by physical displacement, invasion, as well as induction of functional reorganization. Thus, the results of MSSEP PRT can be influenced by lesion location in 2 ways. First, mass effect on and distortion of perirolandic anatomy can result in suboptimal positioning of the recording strip electrode in relationship to the CS, increasing the time required

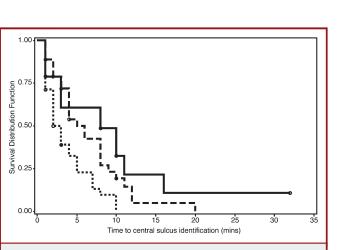


FIGURE 2. Kaplan-Meier curves comparing the rates of achieving central sulcus (CS) localization in 3 groups: far (dotted line), intermediate (dashed line), and near (solid line). Within each group, the circles represent censored cases in which CS localization was aborted. CS localization via the median somatosensory evoked potentials phase reversal technique is significantly delayed if the lesion is in close proximity to somatosensory cortex and to a lesser but still significant extent if at an intermediate distance.

for successful CS identification. Second, a postcentral gyrus lesion can directly affect the function of the somatosensory cortex and thus the generation of SSEPs, thereby making them more difficult to reliably detect. We found that mass effect on perirolandic anatomy (intermediate group) and, to an even greater extent, close proximity of a lesion to somatosensory cortex (near group) significantly delay localization of the CS. These effects are most likely caused by architectural deformation of perirolandic anatomy and physiological changes in infiltrated cortex, respectively. Our results are in concordance with previously published work by Romstock et al²⁴ showing that this method was less successful in cases of pericentral pathology.

Lesion pathology was another important determining factor for time to successful mapping. The normal function of eloquent cortex, including generation of robust evoked somatosensory responses on stimulation of peripheral nerves, may be disturbed by the presence of a lesion that has a high likelihood of destroying

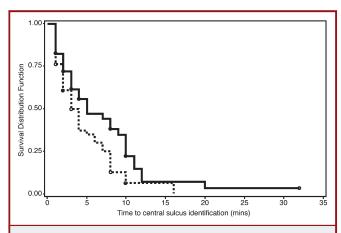


FIGURE 3. Kaplan-Meier curves comparing the rates of achieving central sulcus (CS) localization in the group with less destructive pathology (dotted line) vs the group with highly destructive pathology (solid line). Within each group, the circles represent the censored cases in which CS localization was aborted. CS localization via the median somatosensory evoked potentials phase reversal technique occurs more slowly in the group with more destructive pathology.

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functional neurons (eg, poststroke gliotic changes, high-grade gliomas). We found that such destructive pathologies lengthened mapping time compared with less destructive pathologies such as low-grade gliomas, metastases, and neurodevelopmental lesions.

Another factor examined in this study was the degree of cortical suppression, as appreciated by the presence or absence of a burst suppression pattern on the ECoG. Cortical suppression appears to influence other electrophysiological mapping techniques.¹⁷ The dampening of transmission of sensory information in the cortex could presumably affect the phase reversal method. However, we found no significant effect of cortical suppression on the rate of CS localization. This result is in accord with previous findings, in which different types of anesthetic agents did not affect the difficulty of CS localization.²⁵

Age has been previously shown to influence intraoperative electrophysiology, but primarily through alteration of anesthetic pharmacokinetics and cortical suppression.^{13,26-30} In our study, the age of the patient did not have any demonstrable effect on the rate of CS localization, quite possibly because our patient population (age range, 7-78 years) did not include very young children or octogenarians.

The impact of epidural (vs subdural) recordings on obtaining informative results was not significant. Given the significant thalamic amplification of SSEPs triggered by peripheral nerve stimulation,³¹ these results are perhaps not surprising. On the other hand, they do provide reassurance that successful CS localization is not contingent on subdural electrode placement, which may be difficult (eg, reoperations with adherent dura) or unnecessary (eg, epidural stimulator placement). Additionally, in cases in which the CS is not exposed, its location can be confirmed by sliding the recording strip epidurally rather than subdurally, thereby reducing the chance of tearing bridging veins.

Limitations of our study include its retrospective nature, as well as the imperfect way of categorizing the proximity of a lesion to somatosensory eloquent cortex. The latter was done indirectly by measuring the distance of the lesion/edema margin to the CS. It is possible that this is not the most precise way to appreciate such anatomic relationships, especially given limitations of imaging resolution, and even more so in cases of functional reorganization of eloquent cortex. Furthermore, a potential criticism of our approach could be that CS localization via MSSEP PRT is redundant and therefore an unnecessary waste of time if motor mapping via direct cortical stimulation is also going to be performed. In our experience, however, MSSEP PRT reduces the time spent performing direct cortical stimulation, thereby increasing the precision and safety of the latter. This is particularly true in cases in which there is abnormally increased baseline cortical excitability (eg, patients with epilepsy), leading to higher risk of seizures triggered by electrical stimulation. In such cases, PRT directs electrical stimulation toward the regions most likely to harbor eloquent motor cortex, thus decreasing the risk of unnecessarily prolonged stimulation at unnecessarily high currents. Whether the overall time requirement and success rate using a combination of MSSEP PRT and direct stimulation is improved is the subject of further investigation.

CONCLUSION

The MSSEP PRT is effective for CS mapping and only marginally lengthens operative time. Increased time requirement for CS identification can be expected for highly destructive pathologies in proximity to the presumed location of the somatosensory cortex. Reliable CS localization does not require subdural electrode placement and is not significantly influenced by the presence of deep electroencephalographic cortical suppression.

Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

A ccurate localization of motor cortex minimizes risk of postoperative deficits. This reports describes technical and clinical issues about surgical motor cortex localization using somatosensory evoked potentials. The findings about burst suppression are useful to surgical teams who wish to use that deliberately, while still maintaining the ability to identify motor cortex. Although not unexpected, good research here does confirm that both are mutually compatible. The authors offer reassurance that the technique added little time to their cases.

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The author's current data demonstrating that proper implementation of the phase reversal technique for locating the central sulcus can add little time to the surgical procedure while locating this critical neural structure. More importantly, they offer data on why this mapping technique may or may not be beneficial in certain cases. This is why it is important for the monitoring team to understand the underlying pathology of the surgical patient. In addition, the data presented by the authors may dictate the order in which a mapping technique should be used. The authors demonstrate that mass effect and distortion of perirolandic anatomy is one of the reasons for increased time and may dictate the order or choice of mapping technique, ie, distortional pathologies may be cause for directly going to motor mapping to minimize localization time. The data presented in this article should improve the way in which the surgeon adds the results of each technique to decision processes in the operating room.

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