Local cortical function after uncomplicated subdural electrode implantation

Laboratory investigation

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Object. Although subdural electrodes are routinely used to map regional brain function, it is unknown if the presence of these implants hinders local cortical function. The authors used psychophysical methods to measure the effect of uncomplicated electrode implantation on local cortical function.

Methods. Local field potentials were used to map receptive fields (RFs) for subdural electrodes that were unilaterally implanted on early visual cortex in 4 patients. After electrode implantation, patients did a task that required them to detect an orientation change in a flashing visual stimulus that was presented either inside the mapped RF or outside the RF in the diametrically opposite portion of the other hemifield. The size of the orientation change was varied to span a wide range of behavioral performance. Psychometric curves were generated by fitting behavioral responses to a logistic function. The threshold was defined as the point at which the fitted function crossed 50% detection.

Results. Data were well fit by the logistic function in all 4 patients for both RF and non-RF conditions. None of the volunteers tested showed a statistically significant difference in detection threshold, reaction time, or in the slope of the psychometric function for stimuli presented inside or outside the RF.

Conclusions. Subdural electrodes implanted for extraoperative monitoring do not impair psychophysical performance for a task based on stimuli lying within the RF for recording electrodes. This finding suggests that these electrodes can be used reliably for accurate assessment of regional neurological function.

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Key Words • brain function • brain mapping • electrophysiological monitoring • psychophysical measurement • vision

Subdural electrodes are useful and important tools for functional mapping of the human brain. Typically, these electrodes are surgically implanted on the cortical surface in patients who are then studied in an epilepsy monitoring unit for several days (usually ≤ 2 weeks), both to identify epileptic foci1,2 and to localize critical functional areas.3 Although the clinical purpose of these studies is to facilitate the planning of a subsequent neurosurgical resection, invasive recordings from subdural electrodes are also a unique and valuable source of scientific information about the fundamental organization of the human brain,4 and they serve as a useful complement to the noninvasive techniques such as functional MR imaging, event-related potential recordings from scalp electrodes, and magnetoencephalography that are currently the primary methods used to study human brain function.

Implantation of subdural electrodes on the cortical surface is associated with a noteworthy risk of neurological complications, particularly when a large number of electrodes is implanted. A small subset of patients with semi-permanently implanted subdural electrodes exhibit clear focal neurological deficits, such as aphasias, apraxias, hemipareses, and visual field defects, which typically resolve fully after electrode explantation.5,12 Some of these deficits are attributable to extraaxial fluid collections that result in mass effect or to the implantation of large electrode grids that in themselves may cause mass effect.17,25 There is also histopathological evidence that the subdural electrodes can induce an inflammatory reaction in underlying cortex.27 Nonetheless, these electrodes are used not only for clinically useful brain mapping but also for more detailed studies of a wide range of functional neuroanatomical systems in humans, including studies of audition,2 vision,7,80 language,5,12,17 memory encoding,24 somatomotor function,6,9 somatosensory function,20 and multisensory integration.18,22

Generalizing the inferences drawn from these and other studies demands that the subdural electrodes do not significantly alter the function of neurons in their vicinity. Although it is clear that patients with clinical deficits or radio-

Abbreviations used in this paper: CT = computed tomography; MR = magnetic resonance; RF = receptive field.
graphic evidence of mass effect after electrode implantation are not ideally suited for detailed brain mapping studies, even in the absence of radiographic evidence of complications or clinically evident neurological deficits, it is plausible that the electrodes may interfere substantially with the function of neurons in their immediate neighborhood, and that asymptomatic patients may have subtle dysfunctions that could confound attempts at fine mapping of cortical function. Performance of tasks near behavioral thresholds is especially sensitive to potential subclinical impairments. Nevertheless, no previous reports have examined the possibility of unrecognized impairments by studying threshold performance with the aid of stimuli that are represented by neurons in the vicinity of subdural electrodes. In an effort to answer this question, we examined the impact of subdural electrodes on patient performance in a visual discrimination task at the psychophysical threshold.

Materials and Methods

The Baylor College of Medicine Institutional Review Board approved all procedures used in this study. The participants were patients with poorly localized intractable epilepsy who underwent insertion of multiple standard clinical subdural strip electrodes (Ad-Tech) for localization of seizure onset. In all patients, there was no clinical or radiographic evidence of local mass effect or other complications, and a strip electrode was positioned on the cortical surface of one occipital lobe. A postoperative imaging study obtained in one of the patients is displayed in Fig. 1. Only patients with preoperatively intact visual fields and normal corrected visual acuity were included in this study. Participants included 1 male and 3 female patients who ranged from 17–41 years of age. Postoperative CT scans obtained on the morning after implantation confirmed the absence of a structurally evident complication in all patients. The location of recording electrodes was determined by fusing the postimplantation CT scans with preoperative MR images. Receptive field locations used in this study were mapped from electrodes positioned on anatomically normal–appearing cortex and on a location that was determined to be outside the zone of seizure onset, as determined by ictal recordings captured during video electroencephalography monitoring with the implanted electrodes in place. Experiments took place in the epilepsy-monitoring unit within 1 week of electrode implantation (postimplantation Days 1, 2, 4, and 7, respectively, in the 4 patients). During experimental sessions, clinical monitoring was interrupted. Patients were seated on their hospital beds facing a calibrated liquid crystal display video monitor (Viewsonic-VP150; 768 × 1024 pixels) at a viewing distance of 57 cm, with a resulting display size of 30.5 × 22.9". Surface electrodes record from a local region and can provide small, well-defined spatial RFs. In each patient, a punctate RF was quantitatively mapped for an electrode located within 2 cm of the occipital pole by using previously described techniques. The patients then performed the peripheral orientation detection task (Fig. 2).

At the beginning of each trial, a fixation point appeared at screen center, followed by stimulus in one hemifield to cue the patient as to the target side for the trial. During each trial, 2 identical small achromatic Gabor patches (sigma 1.5–3" with 0.5–2 cycles per degree, with the same average luminance as the gray background) were flashed on the screen at 2–4 Hz with a duty cycle of 20–50%, with one Gabor patch positioned inside the mapped RF of the selected subdural electrode and the other in the diametrically opposite portion of the other hemifield, well outside the mapped electrode’s RF. A Gabor patch, pictured in Fig. 2, is a circular patch of grating whose contrast decreases gradually from its center. This stimulus is thought to be a nearly optimum stimulus for neurons in early visual cortex. Because the site in the opposite visual hemifield is represented by neurons in the cerebral hemisphere without implanted electrodes, this site served as a good control because it was represented by neurons that were unperturbed by the implanted devices. The orientation of one Gabor abruptly changed by a predetermined amount (1–64") at a random time 1–6 seconds after stimulus onset. In most trials (5 [71%] of 7), the orientation change occurred on the cued side. Patients were instructed to maintain fixation on the cross at the screen center during all trials and to respond to orientation changes in the Gabor patch either in the cued or uncued location with a button press. The allowed response time was 750 msec after the orientation change occurred. Psychophysical data from trials with invalid cues were not used for this analysis, but their presence helped motivate the patients to maintain central fixation. A small number of preliminary trials were used to determine the sizes of orientation changes that were both above and below the patient’s threshold for detection. The formal experiment was then set up with a range of orientation changes that spanned these two preliminary values and allowed statistically significant data collection at and around each patient’s behavioral threshold for detecting the orientation changes.

To determine if subdural electrodes impair psychophysical performance for a task based on stimuli lying within the RF for recording electrodes, we compared the patients’ performance in detecting orientation changes in the two locations in the visual field. Psychometric functions were fitted using psignifit version 2.5.6 software (http://bootstrap-software.org/psignifit/ [accessed October 10, 2007]), which implements the maximum-likelihood method described by Wichmann and Hill.\textsuperscript{20} The goodness of the fit was determined using Monte Carlo methods. Psychometric curves generated for each patient yielded 2 measures of perceptual performance: 1) behavioral threshold values, defined as the point at which the fitted function crossed 50% detection; and 2) the slope of the psychometric function. Confidence intervals for threshold and slope were found by the bootstrap bias-corrected accelerated method implemented by psignifit, based on 10,000 simulations.\textsuperscript{20}

Results

For the occipital electrode recordings used in this study, quantitative RF mapping\textsuperscript{40} revealed a mean RF size of 2.7 ± 0.8" (range 1.9–3.7") and a mean eccentricity of 6.3 ± 1.5" (range 4.3–8.5"). In all patients, performance for the range of orientation changes selected spanned the behavioral threshold. The number of trials for each participant ranged from 83 to 126 (111 ± 20). Figure 3 illustrates the psychometric curves generated for each patient. The data were well fit by the logistic function in all 4 patients, both for stimuli inside the electrode’s RF (solid line, RF condi-

![Fig. 1. Postimplantation scout CT scan demonstrating electrode placement for a typical patient.](image-url)
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![Chart showing orientation change detection task](image)

**Fig. 2.** Chart showing orientation change detection task. Trials began with appearance of a fixation point at screen center followed by a cue (not illustrated) that indicated the probable target location for the trial. Stimuli (Gabor patches) at 2 locations, one of them inside a recording electrode’s RF (*circular dashed line*) and the other at a diametrically opposite position in the contralateral hemifield, were simultaneously flashed on the display at 2–4 Hz. Participants were instructed to press a button when an orientation change occurred in either location. After the brief orientation change, the stimulus returned to the original position.

For each patient, the psychometric curves were used to determine a behavioral threshold value for the orientation detection task. There was little sign of a behavioral effect of the subdural electrode. The mean difference between the threshold for detection of orientation changes outside compared with inside the RF was just 0.05° across patients. The detection thresholds plotted in Fig. 3a were not significantly different for stimuli inside compared with outside the RF for any patient (*p* > 0.08 with Bonferroni correction for multiple comparisons, direct Monte Carlo test). All mean values are expressed ± the standard deviation.

The slopes of the psychometric functions were also derived from the fitted data and compared (Fig. 4b). Again, there were no significant differences between slopes for the RF condition and the non-RF condition (*p* > 0.14, direct Monte Carlo test). Finally, the reaction times for all correct detections were measured and compared. Across all patients, the mean reaction time for stimuli inside the RF (438 ± 66 msec), did not significantly differ from the mean reaction time for stimuli outside the RF (462 ± 41 msec). None of the differences in reaction time for the 2 experimental conditions was statistically significant (*p* > 0.25, *z* test; Fig. 4c).

**Discussion**

Any subtle effects of electrodes on local neurophysiological functioning were expected to lead to poorer performance when stimuli were presented in the RF of cortex underlying implanted subdural electrodes. Nevertheless, our data demonstrate that for a task that requires detection of near-threshold changes for stimuli lying within the RF of a subdural electrode, behavioral performance is not detectably impaired relative to performance of the same task when stimuli are positioned in the contralateral hemifield, outside the RF of any implanted subdural electrodes. Our experiment measured only one specific visual function: the ability to detect small changes of orientation in a punctate stimulus. Visual cortex contains many distinct subregions, each of which has its own representation of the visual field and is thought to be specialized for mediating a different type of visual performance. It is therefore possible that detection of the orientation change depended on activity in later stages of processing. Because the most precise and robust representation of orientation selectivity occurs in early visual cortical areas, we think it is likely that performance in our task depended on activity in these areas. Even if performance of the orientation change detection task is related to activity in later visual areas, these areas probably receive their major inputs from the early cortical areas where our electrodes were located. Thus, in either case, the lack of an effect from subdural electrodes on performance strongly implies that normal cortical processing occurred in the areas beneath the electrodes. Although it remains possible that a different assay of visual performance might have produced a measurable effect, the current re-
Results suggest that many if not all visual functions were essentially unaffected by subdural electrodes that were implanted without apparent complications, and that these electrodes can be used to assess normal neurological function accurately.

Because this study only included patients in whom electrode implantation was uncomplicated, as evidenced by normal neurological examinations and the absence of radiographic evidence of postimplantation mass effect, its results are inherently limited and cannot be readily generalized to patients who exhibit any clinical signs of complications associated with implantation of subdural electrodes. In addition, it is well recognized that the incidence of complications associated with subdural electrode implantation is correlated with the number of electrodes and the size of the electrode array inserted, and that grid electrodes are more likely than strip electrodes to cause compression of the underlying cortex, which may in turn cause cortical ischemia or dysfunction. Our experiments directly tested the effects of strip electrodes, rather than grid electrodes, on local cortical function, and it is possible that even the apparently uncomplicated insertion of grid electrodes may be associated with local cortical dysfunction not typically seen with strip electrodes. Nonetheless, these results offer novel data that suggest that the presence of electrodes on the cortical surface does not usually impair local cortical function, even when assayed using sensitive psychophysical methods.

Whether subdural electrodes are used to map cortical function by recording stimulus-evoked local field potentials or by delivering electrical current for direct cortical stimulation, it is essential that the electrodes do not impair function for them to be used reliably for sensitive mapping of neurological function. In the clinical arena, rough mapping is often all that is needed and this issue may be somewhat less crucial. But, because of their excellent temporal resolution, recordings from subdural electrodes serve as an important complement to functional MR imaging for research in human cortical physiology. When subdural electrodes are used for brain mapping research, the demands for precision may be greater, and it is particularly important that the electrodes do not themselves even slightly hinder local neurological function. Our psychophysical data present the best evidence to date that subdural electrodes do
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Long-term cortical stimulation through surgically implanted subdural electrodes has emerged as a potential treatment for both deafferentation pain\(^2\) and intractable epilepsy\(^5,11,19\). These clinical applications require implantation of electrodes on critical cortical areas, including sensorimotor cortex and language-related areas. Our data show that the presence of subdural electrodes implanted without complication, at least in the short term, does not significantly impair the performance of underlying brain. However, it is certainly possible that a delayed foreign body reaction may occur with a more long-term or permanent implantation, and that might result in late dysfunction. Furthermore, implants used for ongoing cortical stimulation may affect local cortical function in a manner distinct from the effects of electrodes used only for passive recordings.

Conclusions

Performance of a task based on stimuli lying within the RF of a region of visual cortex that directly underlies a subdural electrode is not detectably impaired when measured with sensitive psychophysical methods. This demonstrates that semipermanently implanted subdural electrodes do not routinely impair local cortical function when the devices are implanted without complication, and that these electrodes may be used reliably for accurate assessment of regional neurological function.

Disclaimer

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References


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