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BRIEF COMMUNICATION

Problem of signal contamination in interhemispheric dual-sided subdural electrodes

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SUMMARY

Dual-sided subdural electrodes are used in the localization and lateralization of seizure-onset zones when the area of interest is within the interhemispheric fissure. We designed the current study to test the validity of the assumption that each side of the dual-sided electrodes records from the hemisphere it faces. We recorded with dual-sided strip and grid electrodes implanted in the occipital interhemispheric space in two patients with non-occipital epilepsy during two visual stimulation tasks in which subjects were presented with visual stimuli in the ipsilateral or contralateral visual hemifields. Our findings show substantial contamination of recordings from the opposite hemisphere. Although, as expected, electrodes recording through the falx record faintly from the contralateral cortical surface, they unexpectedly pick up strong signals from the cortex behind them. Therefore, we conclude that these electrodes should not be used for lateralization of the origin of epileptic activity or evoked responses.

KEY WORDS: Subdural grid electrodes, Epilepsy surgery, Electrocorticography (ECoG).

Dual-sided subdural electrodes are placed within the interhemispheric fissure when a mesial seizure focus, with unknown lateralization, is suspected. Ideally, each electrode should record only from the hemisphere it faces, with no contamination from signals in the opposite hemisphere. Patients undergoing presurgical evaluation for epilepsy are also frequently used as subjects in scientific research, which relies on accurate electrographic recordings from the cortex for lateralization of function. To date, no experiments have tested the ability of dual-sided subdural grid electrodes to isolate cortical signals from a single hemisphere in human patients being evaluated for epilepsy surgery.

In order to test the signal isolation of dual-sided subdural electrodes, we chose to analyze signals from the occipital visual cortex where the stimulus–response characteristics and laterality of brain activity can be clearly predicted: Left visual cortex responds to stimuli to the right of fixation and right visual cortex responds to stimuli to the left of fixation (Kandel et al., 1991). By using lateralized visual stimuli, we can determine whether an individual electrode is recording cortical activity only from the hemisphere it faces or whether there is significant contamination from the opposite hemisphere.

METHODS

We analyzed visual cortex responses from two right-handed patients, ages 27 and 32, with refractory epilepsy who required mesial occipital coverage with dual-sided subdural grid electrodes. Invasive recordings in the first patient revealed the epileptic focus to be in the dorsal border zone between the cuneus and precuneus regions. In the second patient, the epileptic focus was located in the lateral parietooccipital region. In both patients the calcarine medial occipital regions were shown to be void of any epileptic abnormalities. We used AD-TECH (Racine, WI, U.S.A.) 8-contact, dual-sided LTM 1X4 strip electrodes (model number DS08A-SP10X-000) in Patient 1 (Fig. 1) and 20-contact, dual-sided LTM 2X5 strip electrodes (model DG20A-SP10X-U00) in Patient 2 (Fig. 2).

The two patients underwent different experimental protocols to test the same hypothesis. Visual stimuli presented on an LCD screen consisted of a high contrast pattern, viewed through either a moving bar aperture (first experiment) or a hemifield aperture (second experiment). The contrast pattern alternated at 7.5 Hz, producing a clear "steady state"

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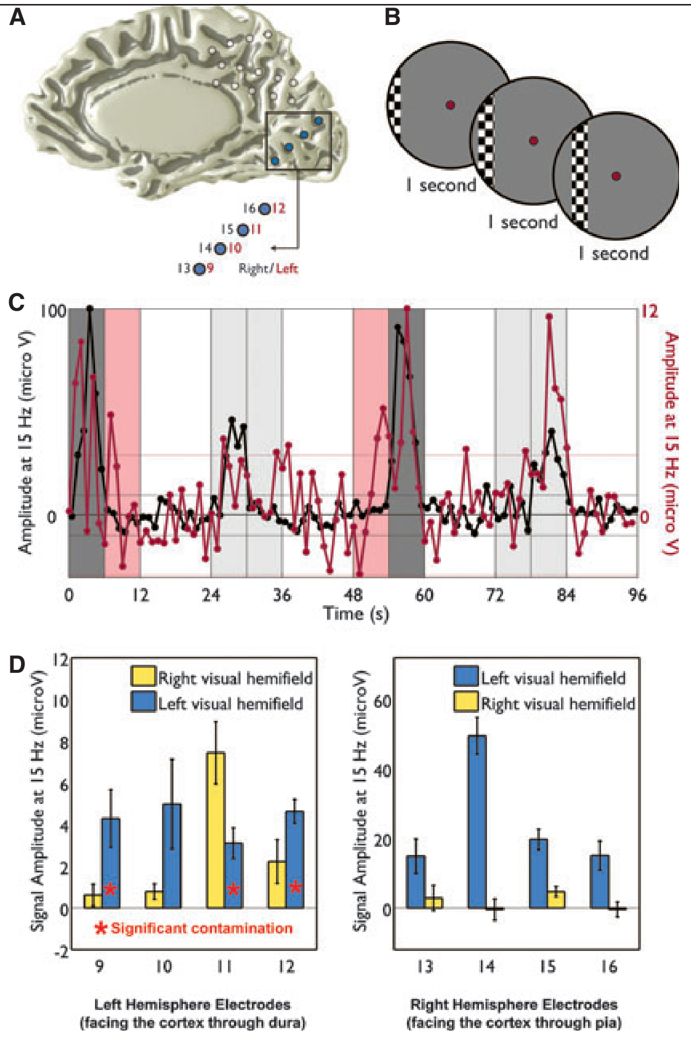

Figure 1.

Experiment 1. (**A**) Locations of interhemispheric electrodes for Patient 1. Electrode pairs used in this experiment consisted of left-facing (numbers 9–12) and right-facing (numbers 13–16) electrodes. Because the grid was placed on the right of the falx, the electrodes facing the left hemisphere (9–12) recorded through dura mater. (**B**) Visual stimuli in this experiment consisted of a checkerboard pattern bar alternating at 7.5 Hz and moving across the screen in 1-s steps. The stimulus bar moved across the screen in horizontal and vertical directions (left-right, down-up, right-left, and up-down) with intervening stimulus blanks in a continuous 96-s sweep. (**C**) The time series is the amplitude in μV of the 15-Hz signal extracted from 1-s windows, averaged across the four experiment repetitions. Portions of the time series are shaded to indicate stimulus positions, with mid-gray regions indicating left visual field positions, red right visual field positions, and light gray upper and lower field positions. Unshaded regions are stimulus blanks (no contrast except for the fixation dot). The dashed lines are the boundaries of the 95% confidence intervals for response amplitudes during the blank stimulus periods. Plots showing a representative time series for corresponding electrodes on opposite sides of the grid are overlapped on the same graph (electrode 14 in black and 10 in red facing the right and left hemispheres, respectively). It is clear that they are highly similar even during the blank periods, indicating that the two electrodes are likely picking up signals from the same cortical origin. The right hemisphere electrodes generally recorded higher amplitude responses as indicated by the larger y-axis values on the left of the time series. For the left hemisphere electrodes, responses are unexpectedly large for ipsilateral stimulus positions. For the right hemisphere electrodes, responses are large for contralateral stimulus periods and near zero for ipsilateral positions, as expected. (**D**) Response amplitude at 15 Hz to stimuli in the left (blue bars) and right (yellow bars) visual fields for all electrodes included in the experiment. Bars indicate the mean amplitude ± SD (standard deviation) across the four experiment repetitions. The right hemisphere electrodes show stronger responses to contralateral stimuli, as expected, whereas left hemisphere electrodes show an unexpectedly larger response to ipsilateral stimuli indicating contamination of signals from the right hemisphere. The right hemisphere electrodes recorded globally higher response amplitudes than the left.

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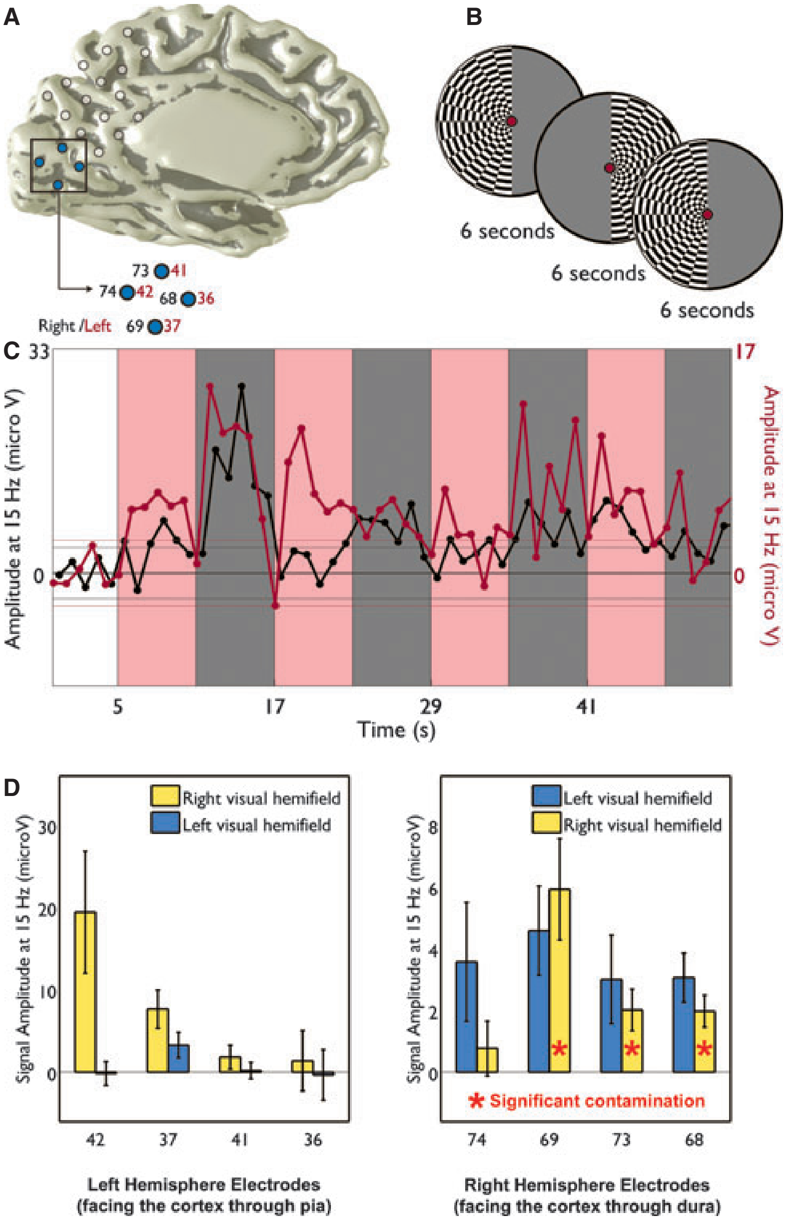

Figure 2.

Experiment 2. (**A**) Electrode locations for patient 2. Electrode pairs used in this experiment consisted of left-facing (numbers 36, 37, 41, and 42) and right-facing (numbers 68, 69, 73, and 74) electrodes. Because the grid was placed on the left of the falx, the electrodes were closer to the left hemisphere. (**B**) Visual stimuli consisted of a hemifield dartboard pattern alternating at 7.5 Hz shown for a duration of 6 s. (**C**) The time series is the amplitude in μV of the 15-Hz signal extracted in 1-s windows, averaged across the three experiment repetitions. The plots showing a representative time series for corresponding electrodes on opposite sides of the grid are overlapped on the same graph (electrode 69 in red and 37 in black). Portions of the time series are shaded to indicate stimulus positions, with red regions indicating left visual field positions and light gray right visual field positions. The dashed lines are the boundaries of the 95% confidence intervals for response amplitudes during the blank preexperiment and postexperiment periods. The left side electrodes were more likely to respond appropriately only to contralateral visual stimuli, but there is a high degree of correlation between the signals recorded by the corresponding electrodes on opposite sides of the grid. (**D**) Response amplitudes at 15 Hz to stimuli in the left (blue bars) and right (yellow bars) visual fields for all electrodes analyzed. Bars indicate the mean amplitude ± SD across the experiment repetitions. Responses from the left hemisphere are larger to contralateral stimuli, as expected. Of the right hemisphere facing electrodes, number 69 responds more to ipsilateral stimuli, but nearly all these electrodes also show a significant response to ipsilateral visual stimuli. These ipsilateral responses indicate cross-hemisphere signal contamination.

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visual evoked potential (Regan, 1977). To ensure fixation at the center of the screen, the subjects were asked to attend to a central target and press a button when its color changed from red to green or vice versa. The color change occurred at random times (average once per 4 s). In the first experiment (Patient 1), the flickering checkerboard pattern bar drifted across the screen in 12, sequential 1-s steps. Four 12-s sweeps were presented in the following order: left-right, down-up, right-left, and up-down. A 12-s blank stimulus (mean luminance gray screen) was presented after each sweep. This 96-s experiment was repeated four times, with short breaks between each repeat. In the second experiment (Patient 2), the stimulus pattern consisted of a high-contrast dartboard pattern also flickering at 7.5 Hz and covered the left followed by the right field of view for 6-s each. The opposite visual field was blank with the same mean luminance as the checkerboard hemifield. This cycle was repeated four times. The 48-s experiment was repeated three times.

In the first experiment, the time series were analyzed in 1-s, nonoverlapping windows because the bar aperture moved once per second. We measured the amplitude of the 15-Hz harmonic by calculating the fast Fourier transform of the raw time series in 1-s intervals. This frequency was selected because a 7.5 Hz flicker pattern has 15 reversals per second and the biggest visual responses are produced by this alternation, concentrating the signal amplitude at twice the stimulus frequency (Regan, 1977). The amplitude at 15 Hz for each electrode was then extracted across the entire experiment, with each time point representing the presentation of a stimulus bar for 1-s. The average response amplitude during the blank stimulus periods was subtracted from the amplitudes of each recorded period. In the second experiment, the data were analyzed in a manner similar to the first in order to produce time series. However, in this case the 6-s preexperiment and postexperiment baselines were averaged and subtracted from the individual time series, as there were no blank stimuli presented during the course of the experiment.

RESULTS

Experiment 1

For the electrodes facing the cortex through pial layer (electrodes 13, 14, 15, and 16), we found large responses when the visual stimulus was in the contralateral hemifield, as expected. The contralateral responses were many times higher than the 95% confidence interval on the noise. When the stimulus was in the ipsilateral hemifield, the responses were mostly within the noise range. A different pattern was observed for electrodes facing the hemisphere through the dural layers (electrodes 9, 10, 11, and 12), in which the responses were larger during ipsilateral than contralateral stimulus presentation. In other words, electrodes facing the left hemisphere through the dural layer responded above the noise level to visual stimuli presented in the left visual field, indicating leakage and contamination of responses from the right hemisphere (Fig. 1C). To quantify this relationship, we calculated the Pearson *r* correlation coefficient between the paired time series. These values ranged between 0.39 and 0.75, indicating a strong correlation between the responses of the electrodes forming a pair despite facing opposite hemispheres. The average contralateral and ipsilateral amplitudes were computed across all the time points in which the stimulus was confined to the contralateral or ipsilateral hemifield, respectively, and averaged over the four experiment repetitions (Fig. 1D). The two time points at which the stimulus overlapped the vertical midline were excluded. One contralateral and one ipsilateral value were computed for each of the four repeated stimulus presentations. Each of the four left hemisphere electrodes showed significant and unexpected responses to ipsilateral stimuli, with three of the four showing larger amplitudes for ipsilateral than contralateral stimuli.

Experiment 2

As shown in Fig. 2, the electrode grid in the second experiment was placed on the left side of the falx. All electrodes facing the left hemisphere showed a selective response to contralateral visual stimuli, as expected. However, the electrodes facing the right hemisphere through the falx showed significant signal contamination. The Pearson correlation coefficient for the four pairs of electrodes ranged from 0.31 to 0.47, indicating a strong correlation within each pair. The average response amplitudes of each electrode to contralateral and ipsilateral hemifield visual stimuli segregated by the hemisphere they faced are displayed in Fig. 2D.

DISCUSSION

Our results have convincingly determined that dual-sided interhemispheric electrodes do not reliably isolate signals from only one hemisphere. Recordings from the visual cortex in the human brain demonstrated that these electrodes, as expected, record only faintly from the cortical surface they face through the falx. However, we also found that electrodes facing the falx pick up strong signals from the cortex behind them.

Our data were obtained from two patients, each undergoing a different experiment to test the same hypothesis. Although we used a dual-sided strip of electrodes in experiment 1, we chose a grid of dual-sided electrodes for experiment 2. Showing the same result using two different experimental paradigms strengthens the validity of our results.

In some cases, even unihemispheric electrodes may respond to an ipsilateral visual field stimulus if they overlay an area corresponding to the vertical midline of the visual field where one would expect some overlap between the left and right visual fields. The significantly increased response amplitude of electrode 37 to ipsilateral visual field stimuli in the second experiment may be partially explained by this phenomenon. It faces bare cortex and is less likely to be affected by recording distance to cortex than the electrodes on the opposite side of the grid. However, this cannot explain the findings in the first experiment. First, ipsilateral activity was found in all the left hemisphere electrodes, covering different areas of the visual field. Second, no region in pericalcarine visual cortex responds more to ipsilateral stimuli than contralateral stimuli, a pattern observed in three of four left hemisphere electrodes. Third, the signal cross-contamination was asymmetric between the paired electrodes, affecting the left hemisphere electrodes more than the right. These electrodes would be expected to cover cortical areas on the two hemispheres corresponding to similar areas of the visual fields. If the response to ipsilateral stimuli were physiologic, one would expect a symmetric response pattern between the two electrodes forming a pair. Lastly, in the first experiment, the bar stimulus covered many different locations within the same hemi-field of view, some of which were distant from the vertical midline and would not be expected to be affected by this effect.

In conclusion, we show that dual-sided interhemispheric electrodes facing the falx may record stimulus-evoked signals from the visual cortex behind them. This will be particularly problematic for epileptiform discharges, which are typically much larger in amplitude and more likely to propagate and contaminate the opposite recording site. Therefore, we urge physicians and researchers to be aware of this limitation when recording from dual-sided electrodes, and conclude that these electrodes should not be used for lateralization of the origin of epileptic activity or evoked responses.

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AUTHOR CONTRIBUTION

J.W., A.M.R., B.W., and J.P. designed research; M.D., A.M.R. and J.P. performed research; J.W., G.N., A.M.R., M.D., B.L.F, and B.W. analyzed data; G.N. and J.P. wrote the manuscript and all authors edited it.

DISCLOSURE

None of the authors have any conflicts of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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