Subdural potentials at orbitofrontal and mesial prefrontal areas accompanying anticipation and decision making in humans: a comparison with Bereitschaftspotential

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Accepted for publication: 19 October 1995

Abstract

Field potentials associated with the execution of a warned choice Go/No-Go reaction task were recorded from prefrontal, supplementary (SMA) and primary motor cortex (MI) by using subdural electrodes in 5 epileptic patients during presurgical evaluation. The choice was between a Go and a No-Go imperative stimulus (S2) in the S1-S2 paradigm. Orbitofrontal and mesial prefrontal areas generated a slow preceding potential before S2 (most likely late CNV), and bilateral mesial prefrontal areas generated a transient potential, most likely related to decision making, upon S2 in both Go and No-Go conditions. In self-paced, repetitive movement, the Bereitschaftspotential was seen only at SMA and MI, but not in the prefrontal area. The present result, therefore, suggests that in humans orbitofrontal and mesial prefrontal areas play an important role in preparation for cognition and in decision making, whereas SMA and MI do so in motor preparation.

Keywords: Contingent negative variation; Bereitschaftspotential; Subdural recording

1. Introduction

Prefrontal cortex plays an important role in making appropriate judgment or decision depending on the circumstances, so that the subject can behave in an optimal way (Goldman-Rakic, 1987; Fuster, 1989). A certain preparatory process for voluntary movements in the cerebral cortex is thought to be represented by a slow cortical negative potential: Bereitschaftspotential (BP) (Kornhuber and Deecke, 1965; Shibasaki et al., 1980). BP is recorded only in association with self-paced voluntary movement. Studies by using subdural recording demonstrated that main generators of BP are primary sensorimotor and supplementary motor areas (SMA), but not the lateral premotor or prefrontal areas in humans (Neshige et al., 1988; Sakamoto et al., 1991; Ikeda et al., 1992, 1993, 1995a, b), although these frontal areas other than primary motor cortex are supposed to play significant roles in preparation for execution of the intention according to the animal studies as well as lesion studies in humans.

Contingent negative variation (CNV), first described by Walter et al. (1964), is a slow negative brain potential. It occurs between two successive stimuli only when the two stimuli are associated with or contingent to each other but not when the two are merely a simple pairing of stimuli. It was suggested that CNV might be useful to measure brain-behavior functions involving cognition, expectancy, preparation, estimation, voluntary motor control, and also judgment process (Tece and Cattanach, 1993). Scalp-recorded CNV was extensively studied, but its generator mechanism has remained unsolved, and especially the role

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S30R 0013-4694(95)00239-1

EEG 95032
of the frontal cortex in generating CNV is still unknown. In addition, from a viewpoint of preparatory process for voluntary movements, the relationship between CNV and BP, or whether BP is one of the components of the late CNV or not, is also to be solved (Tecece and Cattanach, 1993). In the present study, therefore, we recorded BP and CNV in the same subjects from the SMA, primary motor area (M1), and other prefrontal cortices by using subdural electrodes and tried to clarify these questions.

2. Materials and methods

2.1. Subjects and materials

We recorded field potentials directly from the cerebral cortex in 5 right-handed patients with medically intractable partial seizures (4 men and 1 woman, ages ranging from 19 to 48 years with a mean of 35 years). All 5 patients were evaluated for epilepsy surgery using subdural electrodes according to the Cleveland Clinic Epilepsy Surgery Protocol (Morris, 1992). Informed consent was obtained from all patients after the nature and possible consequence of the studies were explained. Four of the 5 patients (patients 1–3 and 5) were discussed elsewhere for another purpose (Ikeda et al., 1993, 1995b, 1996). One patient (patient 5, age 41 years) had an increased signal abnormality on MRI at the left mesial prefrontal area suggesting a tumor, the potentials recorded from which were not used as the results. The other 4 patients had no detectable lesion on MRI.

The potentials were recorded from chronically implanted subdural electrodes. The electrodes were made of stainless steel 3 mm in diameter, and the center-to-center

Fig. 1. An overall location of the subdural strip or grid electrodes on the lateral view of the scalp X-ray film in 4 patients (patients 1–4; 1 = patient 1, 2 = patient 2, 3 = patient 3, 4 = patient 4). Rows of filled, shaded or open circles illustrate separate strip electrodes.
interelectrode distance was 1 cm. This invasive technique can help to identify: (i) the extent of the epileptogenic region, and (ii) the function of the cortex around the epileptogenic region (Hahn and Lüders, 1987). The electrodes were placed at the bilateral mesial prefrontal areas in 3 patients (patients 1-3), at the orbitofrontal area in 2 patients (patients 1 and 4), at the SMA in 4 patients (patients 1-3 and 5), and at the MI in 2 patients (foot and hand area in patients 1 and 2, respectively) (Fig. 1).

2.2. Recording paradigms and data analysis

Two kinds of paradigms were studied in all patients for comparison. One is (i) self-paced, voluntary movement for recording BP (Kornhuber and Deecke, 1965; Shibasaki et al., 1980). Self-paced, voluntary movements (middle finger in patients 1 and 3-5, thumb abduction in patient 2 and foot dorsiflexion in patients 1 and 3) were repeated at an interval of 5-10 sec for movements of one side. The recording conditions were essentially identical to those described elsewhere (Ikeda et al., 1992, 1993, 1995a, b). An averaged waveform from 2.5 sec before to 2 sec after the EMG onset was obtained.

The other paradigm is (ii) a warning choice Go/No-Go task (externally paced, voluntary movement task), during which CNV was recorded. We adopted the paradigm used in the authors’ previous study as follows (Ikeda et al., 1994). A pair of tone bursts of different pitch were presented for S1 (tone burst of 1000 Hz) and S2 with the interval of 2 sec. S2 was either a tone burst of 1500 Hz (Go) or one of 2000 Hz (No-Go). Go and No-Go stimuli were presented in a random order with the same probability. The same motor response as the one used for the BP recording was recorded upon the Go signal in each patient. The EEG segment from 0.5 sec before S1 to 2 sec after S2 was averaged for Go and No-Go trials separately. The Go trials were also averaged time-locked to the EMG onset. A next warning signal was set to be delivered at a variable interval between 3.5 and 7.5 sec after each S2 signal.

In both BP and CNV recording, the subject was told to keep quiet during each recording session and was also asked to postpone the next task movement for several seconds if he accidentally moved prior to the task movement. Before recording sessions, the subject was given a training period until the examiner was satisfied that the subject consistently produced brisk movements preceding and following complete relaxation. One recording session typically lasted 5-6 min. The sessions of BP and CNV were alternately repeated 4-5 times for each with an intermission of a few minutes between sessions.

Cortical recordings were done simultaneously from 40 to 80 subdural electrodes in each patient. All the recordings were performed in the Epilepsy Monitoring Unit concurrently with continuous video-EEG seizure monitoring (Burgess, 1992). The subdural electrodes were all referenced to a common subdural electrode which was (i) not located at the frontal lobe, (ii) inactive in terms of paroxysmal activity interictally as well as ictally, and (iii) negative in motor or sensory symptoms upon electrical stimulation. The bandpass filters applied for EEG and EMG were 0.016-100 Hz and 5-100 Hz, respectively. All of the electrographic output signals were digitized at the sampling rate of 200 Hz/channel and stored on an HP9000/835 for subsequent off-line analysis by a computer program adopting the concept originally described by Barrett et al. (1985).

Trials associated with either (i) significant artifacts, (ii) erroneous response by the subjects, or (iii) movements which were not brisk enough to identify a clear EMG onset, were rejected from subsequent analysis. A total of 112-287 epochs were selected for BP, and 72-127 trials were selected for each Go and No-Go condition of CNV. After it was confirmed that two ensemble averaged EEGs for each condition obtained in each patient were reproducible, then a single averaged waveform was finally made for each condition. As the subdural recording with reference to one of the subdural electrodes does not pick up extracranial artifacts such as EMG and EOG (Ikeda et al.,
1992, 1993, 1995a, b), EOG was monitored only in 2 patients (patients 1 and 5) for confirmation.

2.3. Cortical mapping

Each subdural electrode was individually stimulated to identify cortical function (Lüders et al., 1987). Details of the methodology of stimulation and the subsequent cortical mapping have been described in a series of previous publications of the same group (Neshige et al., 1988; Sakamoto et al., 1991; Ikeda et al., 1992, 1993, 1995a, b). The SMA was identified by its unique responses on the mesial surface, consisting of predominantly tonic motor responses of the upper as well as lower limb and of the...
to this line with motor responses upon stimulation on the right and left sides corresponded to SMA at which somatotopical motor organization was observed. Two electrodes caudal to this line on the right hemisphere had clonic motor responses of the left foot upon electrical stimulation, being consistent with the primary foot motor area. One electrode caudal to this line on the left hemisphere had a sensory response of the right foot upon electrical stimulation, that is consistent with the primary foot area.

3.2. BP and CNV recording

Prior to the onset of self-paced voluntary movements, a slowly rising potential (BP) began 1.5–2 sec before the EMG onset. It was seen in the SMA (Lc6 and Lc7 in Fig. 2B, Rs4 in Fig. 3B; highlighted by a single horizontal bar) and MI limited to one or two electrodes which, when stimulated, elicited contractions of the same muscles as those the subject was voluntarily contracting. These potentials were obtained in all 4 patients in whom recordings were obtained from the SMA or MI. These results were in accordance with previous observations (Nishigae et al., 1988; Sakamoto et al., 1991; Ikeda et al., 1992, 1993, 1995a, b). In contrast, none of the electrodes in the prefrontal area showed similar potentials (Lb1, Lb2, Lf1 and R1 in Fig. 2B, Li2 and Ls1 in Fig. 3B).

In the choice reaction-time paradigm for CNV, both Go and No-Go trials elicited a slowly rising potential between S1 and S2, and at least the latter part of the potential most likely corresponded to the late CNV (Tecce and Cattanach, 1993). It was seen not only at the SMA (Lc6 and Lc7 in Fig. 2C and 2E, Rs4 in Fig. 3C; highlighted by a single horizontal bar) but also at the orbitofrontal (Lb1 and Lb2 in Fig. 2C, Lb1 in Fig. 2E; highlighted by double horizontal bars) and mesial prefrontal areas (Li2 in Fig. 3C; highlighted by double horizontal bars). The late CNV at the orbitofrontal area started just after S1, peaked after S2 (S2-Go or S2-No-Go) and then decayed in 2 sec. This potential had similar amplitude and waveform for hand and foot movements. On the contrary, the late CNV at the SMA was seen only at electrodes where a BP occurred, and its waveform, when averaging was time-locked to the EMG onset, was almost identical to the corresponding BP (Lc6 and Lc7 in Fig. 2B and 2D, Rs4 in Fig. 3B and 3D; all were highlighted by a single horizontal bar).

In both Go and No-Go trials, a clear transient activity was seen following S2 at the orbitofrontal and mesial prefrontal areas (Lf1, Rf1 and Rb1 in Fig. 2C, Lf1 and R1 in Fig. 2E, Li2 and Ls1 in Fig. 3C; all were highlighted by a filled circle). It peaked 270–400 msec after S2. When the same EEGs were averaged time-locked to the EMG onset, the waveforms showed a clear peak just at the EMG onset (Lb1 and Lf1 in Fig. 2D, Li2 and Ls1 in Fig. 3D; all were highlighted by an open circle). Following S1, however, no transient potentials were seen at the orbitofrontal and mesial prefrontal areas.

4. Discussion

The present findings lead to the following two conclusions. The first conclusion is that bilateral mesial prefrontal cortices in humans generate transient potentials in response to dichotomous discrimination tasks which require decision making. It is not just an evoked potential to auditory stimuli because it was not evoked by S1; it was elicited only by S2 at the time when the subject had to decide whether to respond with a motor response or not. The fact that the peak of the potentials identified in the averaged waveforms time-locked to the EMG onset coincided with the EMG onset supports the assumption that this activity actually started before movement onset. Moreover, the peak of the potentials at the SMA occurred with a clear delay. A recent report described a patient with a meningioma compressing the mesial prefrontal area, in whom significantly poor performance of the Go/No-Go task resolved well after resection of the tumor, strongly suggesting that this area has an important role in the decision making process in the Go/No-Go paradigm (Lehmkuhler and Mesulam, 1985). This potential related to decision making is most likely different from the “No-Go potential” described in monkeys (Sasaki and Gemba, 1986) and humans (Sasaki et al., 1993), because (i) the “No-Go potential” is seen only in association with the No-Go situation, and (ii) it is generated from the dorsal bank of the principal sulcus in monkeys and the dorsolateral part of the frontal lobe in humans, according to recent magnetoencephalographic studies (Sasaki et al., 1993).

The second conclusion is that orbitofrontal and mesial prefrontal cortices in humans generate slow potentials in the period of uncertainty and anticipation preceding the forthcoming informative stimulus. It most likely corresponds to at least a part of the late CNV (late CNV “proper”). There have been controversies as to whether the late CNV as a whole or at least a part of it is simply a BP (Tecce and Cattanach, 1993). We recently described a patient with a discrete cerebellar efferent lesion in whom no BP at all but a clear fronto-central dominant late CNV was seen (Ikeda et al., 1994). It suggests that the so-called late CNV “proper” most likely arises from the frontal areas other than motor cortices. The present results also suggest that the scalp-recorded CNV is actually a sum of two potentials, namely the slow preceding potential before S2 generated in the prefrontal region, and the BP generated in the SMA and MI.

It is unlikely that these prefrontal potentials, especially those at the orbitofrontal area, have been documented in the previous scalp-recorded studies since the cerebral cortex has a convoluted surface with its orbitofrontal and mesial prefrontal surfaces buried. The present recording has significant limitations because of limited coverage of the cortex. Nevertheless, it clearly shows that the prefrontal cortex participates actively in the cognition process,
including the decision making process, related to voluntary movements.

In the present study, we had no patients in whom subdural grid electrodes were placed over the lateral prefrontal cortex. Therefore, it is unknown whether the lateral prefrontal area in humans also generates the so-called late CNV “proper” or not.

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