Potentials Associated With the Go/No-Go Paradigm in Traumatic Brain Injury

Avinoam Nativ, PhD, Jo-Anne C. Lazarus, PhD, Janet Nativ, MSc, Jon Joseph, PhD


* Surface event-related potentials associated with visually triggered movements (Go) and the inhibition of planned movements (No-Go) were examined in seven healthy subjects and five postacute traumatic brain injured (TBI) subjects. Analysis showed that the cortical potential P1-N1 was similarly affected by condition in both the control and TBI groups. Although TBI subjects showed smaller P1-N1 amplitudes (Go = 2.91uV; No-Go = 3.95uV; p < .03) relative to control subjects (Go = 4.82uV; No-Go = 6.03uV; p < .03), both groups showed larger amplitudes in the No-Go condition. A bipolar lead (C3'-C3") over the sensorimotor cortex showed a reversal of polarity between Go and No-Go conditions which was synchronized with the EMG activity in all control subjects. This signal reversal and timing of potentials was absent in four of the five TBI subjects’ waveforms, suggesting difficulty in sensorimotor processes associated with movement control. In addition, TBI subjects displayed a number of atypical stimulus-locked waveforms, which are discussed relative to the specific functional impairments of individual subjects. The results highlight the potential usefulness of such paradigms as the Go/No-Go procedure in the analyses of electroencephalographic waveforms and of the effects of TBI.

© 1994 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation

Motor impairments after brain trauma frequently include slowness and apparent difficulties with inhibiting or reversing inappropriate motor commands. Brain potentials associated with the arresting of a preplanned movement have been studied in both animals and human subjects using the Go/No-Go paradigm. In this paradigm, the subject is required to produce a response to a given signal (ie, green light) as fast as possible and to arrest or inhibit that same response when a different signal (ie, red light) is given. Typically, the potentials of most interest in such investigations have been those of the early positive-to-negative (P1-N1) complex which peaks 100 to 200msec after the sensory signal. The precise nature of this complex, that is, whether it is sensory- or movement-related, is still subject to debate. Recent data suggest that these cortical potentials are in fact related to the inhibition of movement in control subjects. The question arises as to whether similar physiological correlates of movement control could be helpful in the investigation of motor impairment associated with brain trauma.

Data from control subjects suggested that the enhanced P1-N1 and N2 (a second negative deflection) components in the No-Go paradigm were dependent to a large extent on the response priming of subjects: Enhanced P1-N1 and N2 were most apparent when fast responses were planned and then arrested. Of additional interest in the previously mentioned study was the finding of a positive surface potential associated with the motor response in a bipolar channel depicting the activity over the contralateral sensorimotor area. This positive potential was synchronized with the EMG activity in the Go condition and reversed polarity when movement was arrested in the No-Go condition.

Although movement-related potentials are more difficult to investigate in traumatic brain injury (TBI), largely caused by cocontraction of antagonist muscle groups and to a less clear onset of the EMG activity in these subjects, their potential for identifying cerebral abnormalities associated with movement disorders is good. Although the nonhomogeneity of this subject population makes interpretation of the data somewhat more difficult, the identification of electrocortical measures which are sensitive to specific impairments is important. Investigating the brain activity associated with the initiation and inhibition of movement in TBI subjects, who typically are impaired in initiating as well as inhibiting fast movements, may provide a more thorough understanding of the mechanisms of motor impairments in the brain-injured. In this study, the questions of primary interest were (1) do TBI subjects exhibit No-Go potentials? and (2) can the pattern of brain activity in the Go/No-Go paradigm be linked to specific motor impairments in these subjects?

METHODS

Subjects

Five postacute TBI subjects (4 men, 1 woman) ranging in age from 18 to 31 (mean age = 26) and seven control subjects (4 men, 3 women) ranging in age from 21 to 43 (mean age = 34) served as subjects for this study. The table presents the relevant information regarding the TBI subjects.

Procedures

Subjects were seated comfortably in a chair and held a trigger in one hand. The control subjects and the two right
hemiparetic TBI subjects (A and B) used the right hand for the experimental task. TBI subjects C, D, and E were left hemiparetic and held the trigger with the left affected hand. A light emitting diode (LED) was placed approximately 2m away from the subject in the center of the visual field. The subject was instructed to respond "as fast as possible" to a green light and to inhibit that response when a red light came on. The movement on Go trials consisted of flexion of the index finger on the trigger. The green and the red lights were randomly displayed (50 green: 30 red) for 7,000msec each. An auditory warning signal preceded the visual signal by 2 seconds. Stimulus presentation was controlled by the experimenter and occurred when the subject appeared ready (an average of every 3 to 4s) and was not showing any eye movements.

**Recording**

Five channels of electroencephalographic activity (EEG), were recorded for 1.5 seconds (500msec preceding the visual signal and 1,000msec following it) and stored for averaging. Silver electrodes were placed on the scalp according to the 10/20 international system at frontal positions (Fcz) (midway between the vertex of the 10-20 system [Cz] and the frontal midline [Fz]), C3'/C4' and C3'/C4'' (1.5cm anterior and 1.5cm posterior to C3/C4, respectively), occipital midline (Oz), left parietal cortex (P3), and right parietal cortex (P4). This montage allowed for four monopolar channels referenced against linked ears (A1 + r) and for one bipolar channel (C3'/C3 or C4'/C4'). The bipolar channel recorded brain activity over the contralateral sensorimotor cortex. For control subjects and for TBI subjects A and B, the C3'-C3" configuration was used. The C4'-C4 configuration was used for TBI subjects C, D, and E who performed the experimental task with their left, paretic hand. A ground electrode was placed on the forehead (Fpz). Electrode impedance for the EEG recording was kept below 3kΩ. Electro-oculographic activity (EOG) was recorded to detect eye movement artifact. Electromyographic activity (EMG) from the flexor digitorum superficialis muscle and movement onset, as detected by the closure of the trigger switch, were also recorded on line. The interval between the imperative signal and peak EMG wave defined the reaction time of subjects in the present study. Peak EMG was used rather than EMG onset because it is more easily defined in TBI waveform.

EEG and EOG signals were band-pass filtered (0.045 to 120Hz) and amplified by a Nicolet 1A98 EEG machine before digitizing. EMGs were recorded from prespaced (2.5cm) Ag-AgCl surface electrodes. The signals were pre-amplified at the source, full-wave rectified and band-pass limited from 40Hz to 4KHz (2.5msec averaging time) before digitizing. An Aicor 1100 digital computer was used to collect data, digitize and record the trigger closure, the flexor EMG, the EOG, and the five EEG signals.

**Analysis**

All signals were aligned with the visual stimulus and averaged as Go or No-Go trials (stimulus locked potentials). False responses were not included in the analysis (ie, responding to a red signal or not responding to a green signal). Individual trials were inspected for eye movement artifacts before averaging and when present eliminated from the analysis. The measures of interest were the P1 - N1, N2, and the activity over the central sulcus, ie, between the primary motor and sensory strips. These selected parameters were then subjected to three way analyses of variance (ANOVA) with one grouping factor (subject population) and two within subject measures; condition (Go/No-Go) and electrode location (Fcz, Oz, P3, and P4). Additional ANOVAs were conducted to further explore event-related potentials associated with a particular lead or with a particular subject group.

**RESULTS**

The typical waveforms associated with a simple warned reaction time (RT) paradigm in a control subject are illustrated in figure 1A.
THE GO/NO-GO PARADIGM, Nativ

Fig 1—(A) Surface potentials from a single control subject associated with visually triggered right finger flexion (average of 50 trials). One and a half seconds of brain activity were recorded; 500 msec preceding the imperative signal (which is marked by an arrow) and 1,000 msec following it. The stimulus-locked waveforms illustrate the early P1-N1 complex. The Fez electrode was placed over the frontal cortex half way between Fz and Cz. P3, P4, and Oz monitored the surface activity over the left parietal, right parietal, and occipital cortex, respectively, according to the 10/20 international system. All monopolar channels were referenced to linked ears. The C3’-C3” bipolar channel depicted potential differences between the sensory and the motor cortices controlling the hand. EMG from flexor digitorum superficialis, the trigger deflection and EOG activity associated with the initiation (thin line) and inhibition (heavy line) EMG signal (green light for Go and red light for No-Go) is indicated by the arrow. Note the separate negative potentials, N1 and N2, in the No-Go condition, particularly in the Fez channel but present also over the P3. Negative potentials show as upward deflections. (Reprinted with permission.)

Fig 1B shows typical brain activity associated with the Go/No-Go paradigm and highlights the principle components. The data from the control subjects suggested two separate negative components within the first 250 msec following the imperative signal, the N1 sensory peak (average latency of 170 msec) and a second negative deflection, N2 (average latency of 224 msec). The latter potential, which may very well be the inhibitory No-Go potential suggested by Gemba and Sasaki, had longer latencies in the parietal and occipital leads (235 to 245 msec) than in the Fez lead.

Not surprisingly, subjects with TBI were slower to respond to the imperative signal than the control subjects (mean RT for TBI subjects = 480.6 msec; mean RT for the control group = 297 msec, p < .01). Separate analyses for the two experimental groups confirmed that the experimental manipulation (condition) had the same effect on the TBI and the control subjects. The P1-N1 peak to peak amplitude was larger for No-Go trials than for the Go trials in both groups (for the TBI subjects: Go = 2.91 μV; No-Go = 3.95 μV; F = 11.4 df = 1.4 p < 0.03; for the control subjects: Go = 4.82 μV; No-Go = 6.03 μV; F(Fez) = 7.37 df = 1.6 p < 0.03). A significant effect of electrode location in the P1-N1 amplitude analysis was evident in both overall (F = 4.29; df = 3.30; p < .01) and separate (F = 6.58; df = 3.12; p < 0.01) analysis for TBI subjects. The most prominent P1-N1 amplitudes were recorded in the Fez and P4 leads (average amplitudes for the overall analysis: Fez = 4.90 μV; Oz = 3.37 μV; P3 = 4.45 μV; P4 = 5.50 μV; for the TBI subjects alone: Fez = 4.64 μV; Oz = 1.92 μV; P3 = 2.85 μV; P4 = 4.31 μV).

Atypical Waveforms in TBI

Figure 2 shows the electrical activity in the bipolar (C3’-C3”, or C4’-C4”) lead in two representative control subjects and in the five TBI subjects. This lead is a less conventional channel which records polarity differences across the central sulcus over the cortical representation of the active hand. In the control subjects, the EMG activity was associated with a negative potential (thin line). In contrast, the waveforms associated with the No-Go condition typically displayed a positive deflection (heavy line) at the C3’ C3” lead. In Go trials, the negative deflection was aligned with the EMG burst (see fig 2). In comparison, the positive wave of the No-Go trials occurred during the same time frame that the EMG burst would have occurred had the trial required a response (as shown in fig 2).

Unlike the control subjects, in four out of the five TBI subjects tested, the cortical activity over the contralateral sensorimotor cortex was not synchronized with the EMG burst (fig 2). The Go and the No-Go traces for subject B diverged only about 300 msec after the EMG peak. Even longer sensorimotor delay was evident in the data of subject E and, in addition, the typical negative deflection associated with the Go trials was missing in this subject’s records. Similarly, a positive rather than negative deflection associated with Go trials was evident in the records of subject D. In the latter case, the homatosensory activity preceded the EMG peak by more than 300 msec. The EEG traces of subject C did not show a clear effect of the experimental manipulation; no positive activity was associated with the arrest of movement in this subject’s recordings. The only TBI subject whose data resembled the data from the control subjects was subject A. Interestingly, this subject was also the one whose reaction time was faster than the RTs of the other TBI subjects and within the range of the control group.
**DISCUSSION**

The Go/No-Go paradigm showed differences between the TBI and the control subjects in the task-related brain potentials. The early, stimulus-locked, P1-N1 potential was larger in the No-Go condition in TBI subjects, as it was in control subjects. Whether this finding reflects a normal inhibitory activity in the TBI group, however, is less clear. As has been shown in an earlier investigation, the stimulus-related P1-N1 wave represents perceptual processes associated with the imperative signal and can also be sensitive to the level of preparation reflected in the ensuing reaction time. More recently, it has been sug-
ggested that the No-Go inhibitory potential might share the same time frame with the P1-N1 wave thus influencing its amplitude.

The fact that the P1-N1 amplitude and the N2 amplitude were found to be larger for the No-Go condition in both the control and the TBI group supports a motor rather than a sensory explanation for the P1-N1 amplitude differences. A negative potential peaking around 220msec after the imperative signal would most probably overlap the N1 wave and thus enlarge the P1-N1 complex.

It is not surprising that the Fcz was one of the most sensitive to the experimental manipulation and group differences. The Fcz lead is positioned over the mesial, central cortex which includes the supplementary motor area (SMA). This cortical area has been implicated as a critical system responsible for transducing the intention to act into action. Given such a role, it seems plausible that enhanced activity in this area would be present under conditions where subjects were preparing and executing and/or inhibiting fast movements as seen in this paradigm in both control and TBI subjects.

The most compelling differences between the experimental groups were shown in the analyses of the bipolar lead (C3'-C3'/C4'-C4'). The EEG records from the control subjects in that lead suggest a special role for the sensorimotor strip in the Go/No-Go paradigm. All control subjects exhibited a negative deflection which was synchronized with the peak EMG activity. However, in the No-Go condition the respective time interval showed positive activity. This reversal of polarity at the bipolar (C3'-C3') lead could reflect reciprocal innervation between the contralateral somatosensory and motor cortices: reciprocal inhibition of the sensory area subserving the efferent motor outflow and inhibition in the opposite direction (from sensory to motor strip) accompanying the arrest of movement. As is apparent from the data of the TBI subjects, this functional process may be impaired following brain trauma.

Speculation as to the impaired mechanisms in specific TBI subjects, reflected in the amplitude and latency of the waveforms from the bipolar (C3'-C3') lead, (fig 2) will be offered. Subject B, for example, did not show the typical positive wave associated with the No-Go condition. This subject's records suggest a difficulty in inhibiting preplanned motor activity. In fact, subject B committed the greatest number of errors (9 false Go's on No-Go signal) in the TBI group. In contrast the records of subjects D and E show that the negative waves typical to the Go condition are missing. This may suggest impairments associated with the release of the actual effenter command in the motor cortex.

The relative timing of the sensorimotor activity may also be meaningful. Whereas the positive potentials in the records of subject D preceded the EMG peak by 200msec these potentials considerably trailed the EMG activity in the traces of subject E. Severe spasticity as well as various peripheral impairments could explain the EMG delay in the former case (in fact, subject D suffered from severe joint stiffness). Central impairments of timing mechanisms or abnormal function of the motor strip could account for the cortical activity trailing the EMG burst in the latter case (subject E).

The significance of the typical brain activity over the sensorimotor cortex displayed in the control data and its relevance to reaction time is highlighted by the records of TBI subject A. This subject, who had suffered a relatively focal lesion involving the brainstem and the left occipital cortex, was the fastest and most accurate of the TBI subjects. Similarly, her EEG records (fig 2) showed the opposite deflections for the Go and No-Go conditions characteristic of the control group. This further supports the suggestion that the functional brain activity over the sensorimotor cortex, manifested in the negative and positive potentials typical to the Go and No-Go conditions respectively, is essential to the execution of fast motor acts and to efficient inhibition of such acts.

The use of the Go/No-Go and other motor control paradigms in the analysis of EEG waveforms has good potential in the investigation of the effect of TBI. In addition to the movement-related potentials examined in this study, Rugg and colleagues found the early component of the contingent negative variation (CNV) to be a sensitive measure of dysfunction following closed head injury. Deviations in the temporal and spatial parameters of various waveforms associated with the preparation and execution and/or inhibition of voluntary movement may provide us with a better understanding of the residual motor deficits of those who have suffered a TBI.

Acknowledgment: The authors would like to thank all the subjects who so willingly participated in this study. Human subjects approval for this study was obtained by the Human Subjects Committee of the School of Education at the University of Wisconsin-Madison on September 21, 1989. In addition, all subjects involved in the study gave written informed consent before being tested.

References


Supplier

a. Nicolet 1A98 EEG machine, Nicolet Biomedical Incorporated. 5225 Verona Road, Madison, WI 53711.

b. Acer 1100 digital computer, Acer Technologies Corporation. 401 Charlotte Avenue, San Jose, CA 95131.