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Evoked Potentials: Principles and Techniques

Jan Galik, Ph.D.
Institute of Neurobiology
Slovak Academy of Sciences
Kosice, Slovak Republic

Charles M. Conway, Ph.D.
University of California, San Diego
Anesthesiology Research Laboratory
San Diego, CA

Jan Galik is a graduate of PJ. Safarik in Kosice, Slovak Republic. He finished his Ph.D. at the Institute of Neurobiology, Slovak Academy of Sciences in Kosice. Dr. Galik spent the last two years as a postdoctoral fellow at the Anesthesiology Research Laboratory, University of California, San Diego. Recently, he returned to Slovakia to the Institute of Neurobiology. For more information about the technique of evoked potential recording, contact Dr. Galik by e-mail: galik@ linuxl.saske.sk, by phone: +42-95-765064 or through the Web page at: http://yakshlab.ucsd.edu/ischemia.

CM. Conway carried out his doctoral research in the Laboratory of Psychopharmacolo-gy under the direction of Professor Loy D. Lytle and received his Ph.D. in Psychology from the University of California, Santa Barbara. He now has a postdoctoral position in the Anesthesiology Research Laboratory of Tony Yaksh, Ph.D., 0818, University of California, San Diego, 9500 Gilman Drive, LaJolla, CA 92093-0818 (ccon-way@ ucsd.edu).

INTRODUCTION

Among the many CNS monitoring techniques, evoked potential (EP) recordings represent one of the most effective methods for examination of CNS functions. In contrast to electroencephalog-raphy (EEC) which measures a collection of spontaneous activity, an evoked potential is the recording of neural responses following the presentation of an external stimulus. Neural impulses can be monitored at almost any level including peripheral sensory events, central neural activity and motor responses. For example, after sciatic nerve stimulation the impulse can be tracked at any point along the nerve or spinal somatosensory pathways including arrival at subcortical and cortical structures. EP recordings are directly related to the external stimulus and thus have several advantages of interpretation in comparison to other techniques. The simplicity, high information value, and clinical applicability are all reasons why EP recordings have become an important electrophysiological method in our laboratory. For many years the main subject of our research has been the spinal cord, its physiology and pathophysiology, and the present article is based primarily on our experience with spinal EP recordings.

Basic Principles of Evoked Potential Recording

An EP is a local change in the electrical field of an neural structure that follows the presentation of an external stimulus. Since the amplitude of an EP is similar to that of spontaneous neural activity, an EP can be hidden by these ongoing electrical changes. Consequently, it is difficult to observe an EP in native recordings of electrical activity. The target signal (EP) must be extracted from the "noise" of spontaneous CNS activity. The most frequently used method for EP extraction is the technique of averaging (i.e., summation). Since spontaneous activity is a near random presentation of positive and negative values, the aggregation of these values over time will approach zero. The summation of a sufficient number of sweeps, therefore, results in the practical elimination of noise. Several assumptions must be met to employ this technique: (i) the raw signal is a linear sum of the target signal (EP) and noise (spontaneous activity); (ii) consecutive evoked potentials are stable in shape; (iii) individual components of consecutive EPs appear at the same time following stimulation; and (iv) noise is of random distribution and is not in temporal relation to the stimulating impulse.

Classification of Evoked Potentials

EPs can be classified by various criteria, but the elementary classification is according to the nature of the stimulated pathway or structure (modality of EPs). The basic types of sensory EPs are evoked by stimulation of afferent

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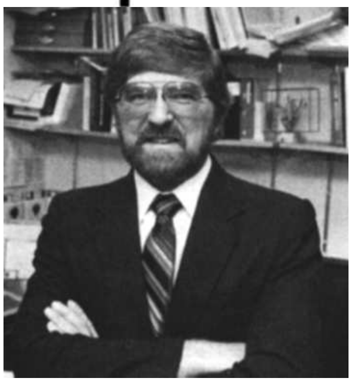

Editor's Column

Winter is here in Kansas City and today the temperature is not supposed to get above 5° F. But we do not have enough snow. At least, that is what I think. I look with envy at the news reports of places like Buffalo, NY and their seven feet of snow. Why can't we have a real snow like that? Perhaps it is because we have our own problems, like a Chiefs football team that did not even make it into the playoffs this year, and a river that floods regularly. I even have my own problems, like a water pipe at home that burst two days ago when the temperature got above 20° F after a few days below zero. Luckily, I was home alone and heard it break loose and got the water shut off before major flooding. But then I had no water until the hardware store opened the next morning and I could get a piece of pipe to fix it with. I just like good snow storms.

The Neuroscience Meetings last November were very good. A lot of you stopped by the David Kopf Instruments Booth to say hi to David and Carol Kopf and congratulate them on the 40th year of the company. They were very pleased at the turnout.

The article in this Carrier discusses many aspects of evoked potentials, and will be followed in the next issue by a companion piece showing EP data from the authors' laboratories. It is notable that this is the second issue authored by scientists outside the US. I invite others to submit articles on their work or techniques.

I wish all Carrier readers a very happy and productive new year. I hope the new year brings you all the excitement you want. (That is the good side of the wish "May you live in exciting times.")

Happy New Year!

Michael M. Patterson, Ph.D.
Science Editor
College of Osteopathic Medicine
The University of Health Sciences
2105 Independence Blvd.
Kansas City, MO 64124-2395
816-283-2308
FAX 816-283-2303

pathways and include: somatosensory EPs, visual EPs, and auditory and brainstem-auditory EPs. Motor EPs are evoked by stimulation of efferent pathways at various levels, (usually by the stimulation of motor cortex or cervical spinal cord) and are typically recorded from spinal cord, spinal ventral horns, peripheral nerves or from the target muscles. One special group of EPs called event-related EPs are recorded from association cortex and can be considered sensory EPs, but the responses are subject to more complex processing than other types of sensory EPs. The most common sites for EP recordings are: peripheral nerves and spinal cord (motor and somatosensory EPs), thalamus (somatosensory EPs), brain stem (brain stem auditory EPs), auditory cortex and auditory pathways (auditory EPs), visual cortex and visual pathways (visual EPs), sensory cortex (somatosensory EPs), motor cortex (motor evoked EPs) and associative cortex (event related EPs).

Parameters of Evoked Potentials

In principle, EPs are a sequence of positive and negative waves. The first basic parameter of each detected wave is its polarity. In the case of monopolar recording, the wave polarity corresponds to the actual voltage polarity (positive or negative) detected by the active electrode. Whereas in the case of differential (bipolar) recording, polarity is a relative value that depends on which electrode is at a given moment more positive or negative with respect to the second one. For example, positive voltage may be recorded by both electrodes but the resulting detected wave can be negative. Since EP recording is a sequence of waves over time, it is possible to determine the time interval from the moment of stimulation to the appearance of each individual wave. This value is referred to as the absolute wave latency. It is often difficult to determine the precise onset of each wave since typically it is hard to find the electrical zero line (isoelectric line) and many waves are joined to other waves without returning to baseline. But this can be overcome by measuring the absolute peak latency, that is, the time interval between stimulation and peak wave appearance. In some applications it is also useful to use inter-peak latencies which are defined as the time intervals between individual peaks. Another important parameter of the EP wave is its amplitude (height), but here to an obstacle exists because of a similar problem with the uncertainty in determining the isoelectric line. However, peaks are easily detected, and so the peak-to-peak (or peak-to-valley) amplitude can be used instead of absolute amplitude. See Figure 1.

The parameters introduced above have varying degrees

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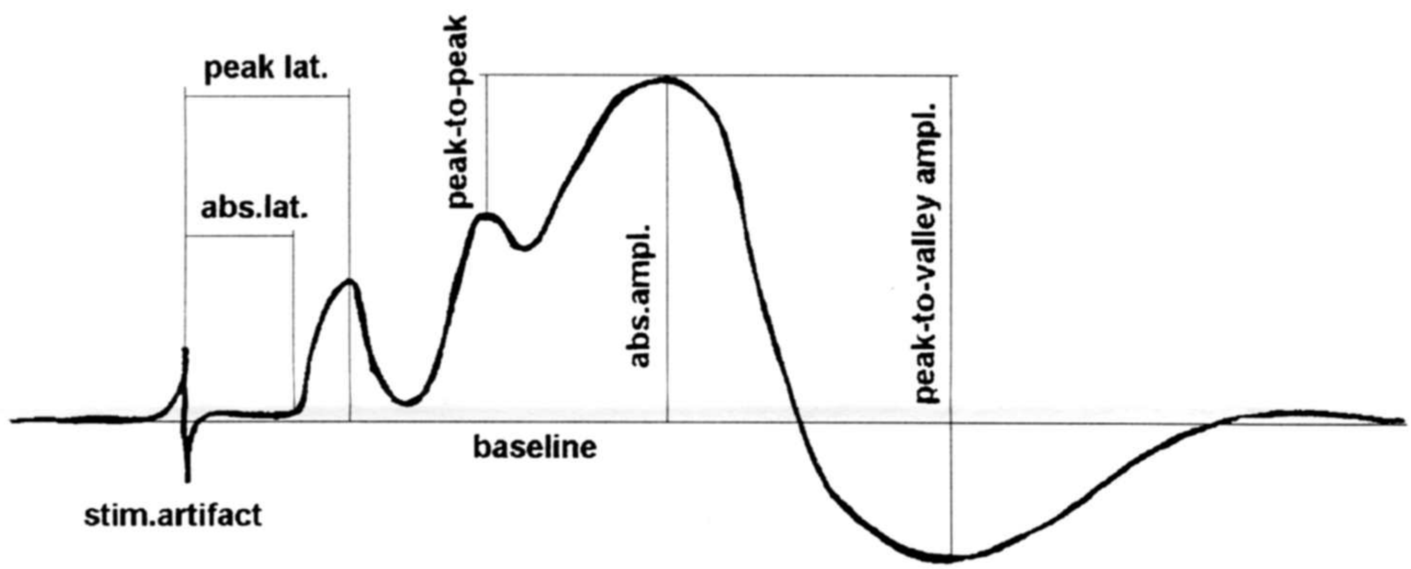

Figure 1. Parameters of Evoked Potentials

of reliability depending upon the specific application. Amplitude, as a value of detected voltage, is sensitive to many factors which are not directly related to the monitored physiological processes. For example, amplitude may vary because of changes in recording electrode impedance (e.g., due to drying, chemical reactions), minor variations in electrode placement (e.g., following muscle twitch), or alterations in stimulation parameters. Latency can also vary, but such changes typically reflect altered physiological conditions such as changes in body temperatureor in the depth of anesthesia. In general, the variability of amplitudes is usually greater than that of latencies. Wave latencies are, therefore, generally considered to be more the reliable parameter for evaluating EP recordings.

It is important to know about the factors which can modify EP parameters and to be aware of possible misinterpretations. Altered EP parameters not only reflect manipulation of the monitored structure, but also are sensitive to changes in systemic physiological conditions such as body temperature, stimulation parameters, and depth of anesthesia. Deviations from normative data can also occur due to subject differences such as age, limb and body size. To avoid misinterpretation, it is critically important to monitor and control factors such as these.

Technical Issues for Recording Evoked Potentials

As follows from the principles of EP recording, the best results can be obtained with higher signal to noise ratios and/or with greater numbers of averaged (summed) poststimulus traces. How-

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ever, collecting large numbers of traces requires extended time periods and makes it more difficult to monitor the dynamics of fast EP changes. Therefore, improving the signal to noise ratio is a more optimal approach for obtaining reliable EP recordings. Unfortunately, spontaneous CNS activity is not the only source of noise for EP extraction. There are also sources of external noise (e.g., power lines, computer monitors) which can produce amplitudes that are higher than the spontaneous signal and might interfere with recording authentic EPs. There are several techniques for maximizing the signal to noise ratio. If the frequency range of noise differs sufficiently from that of the target signal (EPs), then frequency filters can be used to selectively attenuate the amplitude of the noise. Alternatively, if there is overlap in the frequency range of the noise and target signals, then noise can be reduced by the differential (instead of monopolar) recording method. Monopolar recording measures the activity of one active electrode against a reference ground. The resulting output is a nearly exact replica of the electrical field changes that occur in the proximity of the recording electrode. The strength of monopolar recording lies in the correspondence between changes in the electrical field and the recorded trace which makes interpretation of the signal easier. However, it has the liability of recording also the unwanted noise signals. In the differential method, activity is recorded by two active electrodes (placed in different locations) against a common ground, and both signals are subtracted. A remote signal (noise) produces simultaneous changes in both electrodes, therefore the result of subtraction approaches zero (or some constant value). The evoked signal, however, produces a different value at each electrode because it travels by limited velocity to, from or between the two electrodes. Thus, the differential recording method reflects primarily the local changes in impulses (EP) traveling in the proximity of the recording electrodes. Those two features, pronounced elimination of noise and preservation of the useful signal, are the reasons why the differential recording technique is very popular. The price paid for these benefits is that the output is not a true copy of the actual electrical changes. Because of subtraction, the resultant signal is a transformation of the raw electrical events recorded by both electrodes, and interpretation is therefore more difficult than for the monopolar method. In addition to the methods described above, the signal to noise ratio can also be enhanced by decreasing recording electrode impedance, increasing the strength of the stimulating impulse, and positioning the recording electrode closer to the active structure (invasive recording).

Artifacts generated by the stimulating impulse present another technical hurdle for EP recordings (especially for short latency somatosensory EPs). An artifact is a non physiological signal recorded as a consequence of passive flows of the stimulating current through conductive body parts. Stimulating artifacts usually manifest as a large exponentially lowering electrical signal which appears at the moment of stimulation and can be broad enough to cover EP waves or high enough to saturate the input circuits of an amplifier. It is formed by charging and discharging the capacitors formed within an animal's body or in input amplifier circuits. The most effective general method to reduce artifacts is to minimize stimulating current leakage. There are several specific techniques to reduce stimulating artifacts: (i) using an isolated stimulating unit (to prevent current loops to common ground), (ii) differential recording technique, (iii) shortening the duration of stimulation impulse as much as possible, (iv) preventing stimulating electrodes from contacting tissue other then stimulated structure, (v) electrical insulation of stimulated structure (e.g., oil bath), (vi) using bipolar stimulating electrodes where current flows primarily between both electrodes, (vii) placing an additional grounding electrode between the stimulation and recording sites (tripolar stimulating electrodes), and (viii) by changing the geometry of the stimulating electrodes (to change current flow directions in the body volume conductor). Other ways to reduce artifacts are related to the amplifier and include minimizing capacity in the input amplifier circuits (by optimization of analog frequency filters or by using DC amplifier), using special electric circuits, and/or digital filtering. Sometimes electrocardiogram (ECG) artifacts are observed. These can be eliminated by detecting the QRS complex of the ECG signal and delivering the evoking stimulus at a constant delay with the respect to the complex.

Spinal Cord Monitoring

Spinal processing can be examined by EPs at various levels: (i) afferent input to the spinal cord (peripheral nerve, dorsal root ganglia, dorsal and ventral roots), (ii) intraspinal pathways and (iii) arrival of spinal volley at subcortical and cortical structures (scalp recordings).

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Although the functional state of the spinal cord can be examined by measuring both somatosensory and motor EPs, frequently only somatosensory EPs are used. In many applications it has been found that changes in the sensory pathway correspond closely to changes in the motor pathways. Therefore, somatosensory EPs are frequently used to assess the functional state of both sensory and motor spinal systems.

It is almost impossible to enumerate all modifications of spinal EP recording and stimulation techniques. They differ primarily in the type of electrodes used and in the absolute and relative placements of the recording and stimulating electrodes. Electrodes can be grouped depending upon the need for surgical implantation: (i) non-surgical electrodes: skin surface clips or discs, subcutaneous needles, and needle electrodes inserted through skin to the intervertebral space; and ii) surgically implanted electrodes: bone implanted electrodes, hook wire or cuff style electrodes (for peripheral nerve or spinal roots), solid or flexible epidural electrodes, flexible intrathe-cal electrodes, and capillary, needle or wire electrodes (for intraspinal or intragangliaf recording or stimulation). In experimental conditions, selecting among the different recording techniques is fully open, however, in clinical practice it is usually restricted to as noninvasive a technique as possible.

Depending upon electrode placement, the state of spinal functions can be monitored along the spinal cord or on the scalp (both sites can be used for recording as well as stimulation). Some issues related to measurements along spinal cord will be covered first, and those regarding scalp measurements will follow. Recording EPs along the spinal cord provides rather detailed information about specific spinal cord structures. A typical single somatosensory EP trace contains waves that correspond to (i) presynaptic components, (ii) postsynaptic interneuronal components, and (iii) postsynaptic motoneuronal discharges. Changes in the corresponding wave parameters can indicate the level of damage of the particular spinal functional unit. For example, during spinal cord ischemia the spinal interneuronal pool is more sensitive to ischemic insult than any other spinal structures, and therefore changes in the associated waves are the first indicators of spinal ischemia severity. Thus, monitoring of postsynaptic versus presynaptic components of spinal EPs can provide important information. A presynaptic wave reflects the arrival of an impulse at the spinal cord and/or the passing of an impulse traveling along direct spinal pathways. There can be one or more detectable presynaptic waves depending on the different afferent fibers velocities and also on the sensitivity of the electrodes. The postsynaptic waves are generated by second order (or higher) spinal neurons. There are usually several postsynaptic waves that indicate multiple synapses in the recorded pathway and/or reflect the different intraspinal circuits by which the postsynaptic impulses travel. Criteria commonly used to differentiate between the pre- and postsynaptic components are: (i) delayed appearance of postsynaptic waves (latency); and the differential sensitivity of postsynaptic components to (ii) high frequency stimulation (iii) temperature changes, (iv) spinal pharmacological treatment, and (v) to anoxia (or ischemia). Postsynaptic waves are characterized by synaptic delay (-1 ms per synapse), cannot follow stimulation higher than 100-200 Hz (while presynaptic waves remain intact), and disappear almost immediately after anoxic depolarization (presynaptic ones persist for several minutes more).

Scalp-recorded somatosensory EPs reflect the arrival of spinal volleys in the brain stem, sub-cortical and cortical structures. Scalp recordings also contain signals arising from impulses traveling along the nerves and spinal cord called far field potentials (potentials generated physiologically, but spread by physical conduction as electrical current flows in the body volume conductor). This type of recording involves the processing of impulses by cerebral structures and therefore the components of the scalp EPs are sensitive to systemic changes such as the depth of anesthesia, temperature, and anoxia. Scalp EPs can be used as a criterion of spinal cord functions only in those cases where systemic effects are eliminated or taken into account.

This introduction to EP recording will be followed in the next volume of the Carrier by the presentation of our data obtained using spinal EP monitoring in several animal models.

Readings

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2) **Cignek, L.,** *Evokovane potencialy a ich vyuzi-tie v. klinickej praxi.*, Osveta, Martin, 1991.

3) **Moller, A.R.,** *Evoked Potentials in Intraoperative Monitoring.*, Williams & Wilkins, 1988.