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Sub-cortical Visual Evoked Response: Problems Solutions and Clinical Applications

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ABSTRACT

Theoretically, it has been possible to record the occipital Visual Evoked Potential (VEP) by working with non-invasive scalp electrodes. Similar to the Brainstem Auditory Evoked Response (BAER), which successfully addressed the same kind of problem in the auditory system; it will be necessary to adjust the clinical VEP recording protocols to adequately resolve the lateral geniculate bodies and superior colliculi along the bilaterally visual pathways. These are significantly lower amplitude and shorter-duration transitory synaptic events. Therefore, this study aims to purpose the technique to solve the clinical scalp evoked potential recordings for the sub-cortical, synaptic events occurring at the lateral geniculate bodies and superior colliculi along the bilaterally visual pathways.

Key words: Electroencephalogram, visual evoked potential, brainstem auditory evoked response, sub-cortical

INTRODUCTION

Event-related potential (ERP) recordings have bought new insight to the neuronal events behind auditory change detection in visual and auditory perception. ERP components reflect the conscious detection of a physical, semantic, or syntactic deviation from the expected sounds (Tervaniemi *et al*., 2001). The ERP recordings thus allow one to probe the neural processes preceding the involvement of the attentional mechanisms. For instances, ERPs have been recorded that reflect memory traces representing sounds composed of several simultaneous or successive tonal elements (Alain *et al*., 1994; Alho *et al*., 1996; Schroger *et al*., 1996; Sittiprapaporn *et al*., 2005). Previous studies (Naatanen *et al*., 1999; Escera *et al*., 2000; Berti and Schroger, 2001; Takegata *et al*., 2001; Sittiprapaporn and Kwon, 2009) demonstrated that the morphology of ERPs to the additivity of auditory and visual modalities (AuVi) presentation differed to the simultaneously audiovisual (AV) modality. The N2b was followed by a large positive component identified as P3a (Naatanen *et al*., 1999) in the AuVi modality, but little P3a was evident in the AV modality. The occurrence of AV P3a implied the complex interactions between brains processes involved in analyzing several simultaneous deviant features. This component possibly reflects involuntary attention-switching mechanism to deviant stimuli (Escera *et al*., 2000; Berti and Schroger, 2001; Takegata *et al*., 2001).

Historically, in clinical Visual Evoked Potential (VEP) work, it has only been possible, working with non-invasive scalp electrodes, to record the occipital VEP. The earlier, sub-cortical, synaptic events occurring at the lateral geniculate bodies and superior colliculi along the visual pathways bilaterally have not been resolvable in these clinical scalp Evoked Potential (EP) recordings, due

primarily to technical factors inherent in the recording protocols employed (Buchsbaum *et al*., 1981; 1982; Clenney and Johnson, 1983; Celesia, 1985). Questions involving level of lesion have therefore been difficult to address, at least along the section of the visual pathways (optic tracts) from the optic chiasm to the primary visual sensory cortex (Brodmann's area 17 within the calcarine fissure in the occipital lobes), where the first some what difficult to record response occurs at a latency of approximately ≥50 msec (P1). This problem is analogous to that of the mid- and long-latency auditory EP's, which cannot yield any information regarding the status of auditory nerves and lowest-level brainstem structures (Epstein and Brickley, 1985; Frances, 1989). This article then aims to purpose the technique to solve the clinical scalp evoked potential recordings for the sub-cortical, synaptic events occurring at the lateral geniculate bodies and superior colliculi along the bilaterally visual pathways.

VISUAL EVOKED POTENTIAL TESTINGS

Similar to the Brainstem Auditory Evoked Response (BAER), which successfully addressed the same kind of problem in the auditory system, it will be necessary to adjust the clinical VEP recording protocols to adequately resolve these somewhat earlier, significantly lower amplitude and shorter-duration transitory synaptic events (Goff, 1974; Halliday *et al*., 1977; Hjorth, 1982; Owen and Davis, 1985). Specific aspects of the problem are now presented, together with possible solutions as follows:

Problem 1: The synaptic events that are proposed to be recorded occur somewhat earlier than the occipital primary visual sensory cortex response, which is usually rather difficult to record and has a latency of approximately = 50 msec (P1). Also, they have duration significantly shorter than cortical response events. Therefore, it is necessary to:

- **Solution 1:** Employ a shorter recording epoch or window, in order to adequately resolve (minimum = 4 sampling points per waveform) the shorter-duration events likely to be encountered from these sub-cortical areas. For some EEG module like Brain Atlas (BA) III software which is limited to 256 sampling points total and applied to BA 20-channel and EP 4-Channel models

Recording epoch or window: The 32 msec (ISI = 125 μsec)×4 = min. duration 0.5 msec, max. frequency 2 kHz).

- **Solution 2:** Shift this window forward from the stimulus time (BA-III software limits = +/- 255 points), in order to adequately cover the anticipated time of event occurrence

Post-stimulus points (recording delay): +160 points (32 msec epoch, recording from 20-52 msec post-stimulus).

- **Solution 3:** Employ high- and low-pass frequency filters that are appropriate to the duration (or frequency) of synaptic events

Frequency band-pass: The 150-3000 Hz (passing waveform of duration 0.333-6.667 msec).

Problem 2: The synaptic events that are proposed to be recorded are significantly lower-amplitude than cortical events, possibly down into the sub-microvolt level (similar to the BAER, with voltage ranging from 0.1-0.5 μV). Therefore, it is necessary to:

- **Solution 4:** Employ an amplifier Gain setting that is appropriate to recording such low-voltage events, while allowing for secondary (off-line) Display Sensitivity adjustments as may be necessary

Amplifier gain: 300,000.

- **Solution 5:** Average a sufficient number of stimuli to resolve these extremely low-voltage potentials from the massively greater ongoing noise, i.e., EEG activity

Number of stimulus repetitions: 2,000 per trial (×2 trials = Grand Average: 40,000 repetitions).
Problem 3: There appear some additional problems, secondary to the above solutions, i.e., what type of stimulus and what stimulus repetition rate to employ? A clinical EP laboratory test, as distinct from a research paradigm, must be done within a finite and reasonable time frame, as there are usually other test procedures to be done on the patient as well. However, the usual Stroboscopic Flash VEP stimulus is inappropriate. Although the flash duration is measured in μsec, there is a perceptible and undesirable after-flash bounce illumination, which may well contribute an unknown element to the stimulation, altering the response. Additionally, LED Goggles stimulation may be somewhat better to be a sufficiently strong stimulation to elicit a reliable occipital response. They usually require a stimulus duration of at least 10 msec (usually 50 msec), with separate ON and OFF responses (separated by 10-50 msec, with off>on voltage), overlapping, merging, prolonging and confounding the response and confusing the results. Both Stroboscopic and LED Goggles Flash VEP stimulation also inherently lack the capability for use in half-field testing, which is critical to this type of test.

Pattern-Shift VEP would be an adequate stimulus, as the stimulus trigger is delivered to the TV monitor screen electronically, with a measurable but small and fixed delay of a few msec and with no change in overall illumination (Sato *et al*., 1971; Tyner *et al*., 1983; Spehlmann, 1985). However, it is usually done at the relatively slow repetition rate of about 2.2 sec. Assuming little or no artifact, in order to accomplish the recording of 2,000 responses in a 5 min period (2 eyes×2 half-fields×2 trials each = 8 trials total over a 40 min ½-field testing session), a stimulus repetition rate of 6.7 sec is required. Similarly, a full-field testing session at that rate would be done much sooner (2 eyes×2 trials each = 4 trials total over a 20 min testing session). Most importantly, it is uncertain at present whether this rapid a rate could be sustained in a clinical setting and what kind of response it would elicit. However, too rapid a rate might set-up a "Steady-State" response, due to N2 overlap, which is to be avoided. This question will have to be empirically determined. Certainly, such a rate would preclude the use of Strobe and LED Flash stimuli, due to response prolongation. Therefore, it is necessary to:

- **Solution 6:** Employ a stimulus repetition rate adequate to complete the testing session in a reasonable period of time (40 min for 1/20 fields, 20 min for full-fields), while avoiding "Steady-State" VEP overlap of the occipital N2 response component

Stimulus repetition rate: 6.7 per second (ISI = 149 msec, may have to be slower, 5.7 or 5.0 sec).

- **Solution 7:** Employ a type of visual stimulus that is capable of being delivered at the above relatively rapid repetition rate without adverse post-stimulus illumination effects or on/off-merging effects, as magnified by prolonged stimulus duration

Type of stimulus: Between (Electronic [TV Monitor] Checkerboard) pattern-shift.

Problem 4: The sub-cortical synaptic events that are proposed to be recorded are located essentially in the center of the human head, thereby constituting a far-field recording for scalp electrodes. Within the calvarium, they are a bit asymmetrically distributed, with the lateral geniculate bodies being located closer to mastoid M1, M2 (or, alternatively, scalp mid-temporal T3, T4), while the superior colliculi are closer to scalp parietal P1, P2 (or, alternatively, P3, P4), all as compared to scalp frontopolar Fpz. This is similar to the situation with the BAER, where all scalp electrode sites are basically far-field, but with some being slightly closer to the source (M1, M2) than others (Cz). Topographic Brain Mapping (TBM) of the results would suffer from an unacceptable degree of spatial smearing, thereby precluding its' use. However, as with the BAER, these small differences in generator-to-scalp sites' distance and dipole orientation may be turned to good advantage. Therefore, it is necessary to employ a 4-channel EP recording protocol using appropriate derivations to take advantage of the relatively small difference in distances and dipole orientations between sub-cortical generator sites and individual scalp electrode sites.

Channel EP recording montage:

- Fpz-T3
- Fpz-T4
- Fpz-P3
- Fpz-P4
- (GND) Fz

Or, alternatively:

- Fpz-M1
- Fpz-M2
- Fpz-P1
- Fpz-P2
- (GND) Fz

RESULTS AND DISCUSSION

Regarding the issue of providing the results, it should be noted that there is no non-invasive proof possible for the BAER, for any waves following wave I (auditory nerve action potential), due to the degree of crossing and re-crossing of fibers that occurs within the brainstem following auditory nerve entry. Each ear provides differentially auditory sense, frequency and source localization information to primary auditory sensory cortex in both temporal lobes. With the visual system, however, it is possible to separate input from the left and right visual half-fields as well as

upper and lower half-field and even quadrants for each eyes, thereby providing the test by routing visual information differentially to primary visual sensory cortex in only one occipital lobe or, with full-field monocular stimulation belong the standard clinical protocol, to both.

Using full-field monocular stimulation in a subject, it is predicted that the responses would be bi-symmetrical for either eye for each pair of homologous electrodes. However, in the case of half-field monocular stimulation in a normal subject, the prediction would be that voltage/amplitude of the responses would differ as follows for either eye:

- Left ½-field Stimulation: T3 = 0, T4>0, P4>P3>0
- Right ½-field Stimulation: T4 = 0, T3>0, P3>P4>0

It should be noted that the scalp temporal lobe electrode on the side opposite to the route of visual path transmission may not show a total absence of response, but should show one of significantly lower amplitude. In addition, it may show a response of opposite polarity depending on dipole orientation. Also, the amplitudes recordable at scalp parietal electrodes P3 and P4 may be enhanced by the use of P1 and P2 instead, although that may result in a slight diminution of the amplitude difference between them. Ultimately, the choice of recording electrodes, between T3/T4 and M1/M2, as well as between P3/P4 and P1/P2, may wind-up having more to do with the dipole orientation angles of the generator sites than with any small differences in absolute distance separating them from the individual scalp recording electrodes. This will have to be determined empirically.

CONCLUSION

The visual pathways from retina to occipital lobe cortex constitute the longest neuraxis lying completely within the cranium. A variety of clinical conditions are known to affect them including demyelinating disease, tumors, pressure effects from various intracranial space-occupying lesions, intracerebral bleeds, etc. It is to be hoped that this test, if it should prove to be clinically feasible, may reveal that some of these conditions display signature abnormalities by means of which they differentially affect the recording of electro-chemical transmissions along these routes, i.e., by signal blockage, showing desynchronization and inter-hemispheric asynchrony and asymmetry. It may then help to contribute to a better and earlier diagnosis of ailments affecting the human visual system.

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