endophthalmitis can be an argument for the hypothesis that the increase in blood velocity is due partially to a vasospasm of the ophthalmic artery.

Key words: pulsed Doppler sonography, blood velocity, ophthalmic artery, normal subjects, endophthalmitis

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References

Human Presaccadic Spike Potentials

Of Central or Peripheral Origin?

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Electroencephalographic (EEG) activity associated with voluntary and spontaneous saccades were analyzed in 12 normal subjects to determine the influence of volition upon the presaccadic spike potentials (SPs). In addition, two different electrode configurations, of a temporal and a parietal derivation, and two different filter bandwidths were simultaneously analyzed to clarify issues regarding the structure, function, and origin of SPs. An off-line averaging of the pre- and post-saccadic EEG epochs showed distinct spike potentials associated with spontaneous saccades in both the temporal and the parietal locations. Subsequent statistical analyses indicated that the amplitude of the SPs associated with spontaneous saccades was not significantly different from the respective amplitude of SPs preceding voluntary saccades. Independent effects of filter bandwidth and electrode derivation are suggestive of a complex late presaccadic EEG activity. Invest Ophthalmol Vis Sci 31:1923–1928, 1990

Earlier work in our laboratory suggested that spike potentials (SPs, “cortical potentials” preceding eye movements by 10–15 msec) were associated with voluntary, but not with spontaneous, eye movements. Although scalp-recorded SPs initially suggested a posterior parietal origin for this potential, later work with dipole mapping, showed that the origin of SPs was in the orbital region, most probably derived from extraocular muscle activity. A different suggestion
was made by Tsutsui\textsuperscript{4} who used a procedure called “moving topography of evoked potentials” to investigate the origin of SPs. In that study, it was argued that sources in the brainstem, namely pontine burst neurons and motor neurons innervating the extraocular muscles, are responsible for a far-field potential which, due to masking by a frontal negative discharge from the corrugator muscle, is most prominent in the parietooccipital region. McCarley et al,\textsuperscript{5} using topographic methods, also suggested a combined subcortical (lateral geniculate) and cortical (visual cortex) origin for the parietal SP. Our early finding of absent SP for spontaneous saccades is not consistent with an orbital source or even with a brainstem origin for the presaccadic SP. Both the brainstem and orbital structures are part of the eye-movement motor apparatus and are known to be activated for voluntary and spontaneous saccades.

It has been suggested\textsuperscript{1,6} that the inability to detect SPs in spontaneous eye movements could be related to variability in the eye’s velocity signals, which trigger the averaging process (trigger jitter), or to suboptimal recording montage. The primary goal of our study was to reinvestigate SPs preceding spontaneous eye movements under more careful experimental control.

A secondary goal was to determine whether there were differences in the parietal (referenced to linked ears) and temporal (referenced to contralateral parietal electrode) SPs which would indicate differing underlying neurophysiologic processes for the two potentials. Both electrode configurations were, therefore, used simultaneously, and the recorded potentials were compared in tasks involving different levels of voluntary control. In addition, it was thought that the relatively large amplitude and high frequency of the SP should make this sharp wave appear in a narrow window (250 msec) of the on-going, lower frequency electroencephalographic (EEG) activity. Hence, an off-line analysis of single SPs was conducted to clarify issues regarding the structure (eg, monophasic versus biphasic nature) and function of SPs.

\textbf{Materials and Methods.} The data reported in this study are from 12 normal volunteer subjects (five men and seven women) ranging in age from 24–34 yr. All subjects had normal vision or wore spectacle correction. Informed consent was obtained from all subjects after the procedures had been fully explained to them. Evoked potentials were recorded with silver cup electrodes placed on the left parietal cortex (P3) and referenced to linked ears. In addition, the “maximizing recording montage,” as suggested by Riemslag et al\textsuperscript{6} was used. A right temporal electrode (Ta) referenced to a contralateral parietal site (3 cm above and 7 cm behind the auditory canal) constituted this configuration. For both configurations, a midline ground electrode was placed 9 cm above the inion in accordance with Riemslag et al’s procedure.

Horizontal and vertical eye-position signals were recorded using standard electro-oculographic (EOG) techniques with filter settings of 0.5–70 Hz. Both EEG and EOG signals were led to an EEG machine (Nicolet 1A97, Madison WI) where they were amplified, filtered, and stored on streaming tape by a Nicolet Pathfinder I computer. All EEG signals were simultaneously analyzed in two different ways, using both “low-pass” (0.5–70 Hz) and “high-pass” (50–1500 Hz) filter techniques. The taped data were later displayed on a video monitor, screened for eyeblink artifacts, and averaged off-line, using 20–25 epochs of 256 msec each, with 50 msec preceding the onset of EOG deflection. Only rightward saccades were analyzed.

To determine the influence of volition upon the SP, presaccadic evoked potentials were obtained from each subject under two experimental conditions. In the “voluntary” condition, seated subjects were instructed to perform saccades at will between two targets 10° apart (5° to the left and 5° to the right of the straight-ahead position). In the “spontaneous” condition, subjects were not given specific instructions to make eye movements. They were led to believe the instruments were being calibrated and were asked not to move their heads “in order to facilitate the calibration process.” Spontaneous EOG and associated pre- and postsaccadic EEG activity was recorded and analyzed in the voluntary condition. The spontaneous condition was tested first to ensure subject naiveté with respect to the experimental conditions.

\textbf{Results.} Figure 1 shows grand averages of temporal and parietal SPs in both the voluntary and spontaneous conditions. As suggested by Riemslag et al\textsuperscript{6} the temporal derivation was associated with larger spike activity (16 μV on average compared with 8 μV in the parietal derivation). It is further apparent from Figure 1 that the conventional filter setting (0.5–70 Hz) resulted in larger amplitude spikes compared with the SPs associated with the high band-pass filter (50–1500 Hz). As expected from a low-pass analog filter, the spike onset and peak latency were shifted forward (delayed) by 4–5 msec. The SP peaked within 1 msec of the saccade onset and peak latency were shifted forward (delayed) by 4–5 msec. The SP peaked within 1 msec of the saccade onset and peak latency were shifted forward (delayed) by 4–5 msec. The SP peaked within 1 msec of the saccade onset and peak latency were shifted forward (delayed) by 4–5 msec.
Fig. 1. Temporal (left) and parietal (right) spike potentials preceding voluntary (solid line) and spontaneous (dotted line) saccades. The upper traces show grand averages (12 subjects) at high band pass filter setting and the lower traces show the same SPs with "conventional" filter (0.5–70 Hz). Note the biphasic nature of the spike potential in the high band pass filter condition. The vertical line indicates the onset of the EOG signal.
ture of the late presaccadic activity could not be shown when the conventional filter setting (0.5–70 Hz) was used.

The SP amplitude, onset, and peak latencies were recorded for each subject. An additional measure was used in an attempt to represent accurately the volume of late presaccadic activity. “Gross spike amplitude” includes the late antecedent activity in the measurement of spike amplitude. The antecedent potential (AP), a late presaccadic positivity centered over the parietal cortex between 250 and 50 msec before initiation of a saccade, has been recorded by several investigators. Still later (30–40 msec before the EOG signal) a change in slope was detectable in the present data. This late antecedent activity was included in the computation of gross spike amplitude. We measured gross spike amplitude from the onset of a consistent change in slope from the baseline to the peak of the SP. All measurements underwent analysis of variance (ANOVA) with condition (voluntary versus spontaneous), electrode site (temporal versus parietal), and filter (high versus low) as repeated measures.

In the amplitude domain, ANOVA highlighted the difference between the temporal and parietal spikes, the former being much larger in amplitude (eg, 8.1 versus 16.6 μV on average with conventional low-pass filtering; F = 163.5; df = 1,11; P < 0.001), complementing the observation from Figure 1; the SPs associated with low-pass filter (0.5–70 Hz) were larger than SPs associated with the high-pass filter (50–1500 Hz). These results were paralleled in the analysis of the additional measure, gross spike amplitude. The analysis of the latter variable, however, indicated a possible effect of condition; the amplitude differences between SPs in the voluntary and SPs in the spontaneous condition was not statistically significant at the 95% confidence interval (F = 4.066; df = 1,11; P = 0.069). This finding will be discussed further in the next section.

The latency analyses suggested that, in addition to the filter effect (F = 104.59; df = 1,11; P < 0.001), the temporal SP peaks earlier than the spike recorded over the parietal cortex (about 1 msec difference, on average; F = 158.0; df = 1,11; P = <0.001). The spike onset in the temporal configuration was similarly earlier compared with the onset of the parietal activity (F = 17.826; df = 1,11; P = 0.001).

Discussion. A careful, off-line analysis of the presaccadic cortical potentials demonstrated that sharp SPs precede spontaneous and voluntary eye movements. This suggests a motor origin to the SP rather than a cognitive origin associated with volition, as had been proposed in previous work done in our laboratory. A motor origin is more consistent with findings from other laboratories. Our failure to detect a SP associated with spontaneous saccades in a pre-
vious study was probably related to trigger jitter. In this earlier study, a velocity signal was used to trigger the perisaccadic averaging process. A predetermined critical voltage for the velocity spike was required to initiate an average. The critical voltage was set as low as possible, but high enough to avoid averaging on background noise. Because spontaneous saccades are characteristically variable in amplitude and velocity, the time from eye-movement onset to critical voltage, determined by the slope of the velocity waveform, will vary from saccade to saccade. This desynchronization of the averaging trigger may have been sufficient to attenuate significantly the SP associated with spontaneous saccades. Furthermore, the combination of parietal recording location and spontaneous saccades appears to be least favorable for the detection of SPs (Fig. 1). Although we cannot exclude the possibility that the diminution in SP amplitude in the prior study was due in part to smaller saccades in the spontaneous condition, we doubt that saccade size was a major factor because saccades as small as 2.5° produce an SP 50–60% as large as the SP for 10° saccades.

Our data support the idea that several cerebral sources contribute to the SP. Two or more peaks were often recorded before eye movement when the high-pass filter (50–1500 Hz) was used (Fig. 2); these high-frequency peaks were, in most cases, masked by the averaging process. Low-pass filtering smoothed and delayed the multiple high-frequency potentials. Yet, the fact that SP amplitude was larger with low-pass filtering argues for the existence of an independent low-frequency generator. This low-frequency activity may be further separated into low-frequency SP and AP activity. In fact, our data suggest that the inclusion of the AP in the amplitude analysis may reveal a condition effect. Voluntary saccades were associated with larger AP activity than were spontaneous saccades. Tsutsui et al recorded APs before voluntary saccades but not before optokinetic nystagmus; they similarly suggested that the AP “may be related to a voluntary mechanism of the rapid eye movement” (pp. 499). Once again, we cannot exclude the possibility that the reduced gross spike amplitude may be related in part to smaller saccades in the spontaneous condition (an average of 70% of the amplitude in the voluntary condition). This issue will have to be resolved in a separate investigation. However, Kurtzberg and Vaughan found that the AP was significantly larger in saccades triggered by a visual target than in voluntary self-paced saccades like we used. This constitutes further evidence that the low-frequency positive presaccadic activity is closely related to higher order presaccadic processes not reflected in the high-frequency SP, which seems more intimately connected to motor activity per se.

Finally, the SP latency differences between the temporal and the parietal configurations (1 msec earlier temporally, on average) further argues for different (although perhaps related) generator sources contributing to the temporal and parietal potentials. Since the results from mapping investigations are not consistent with frontooccipital electrical propagation of late presaccadic activity, it appears likely that both Tsutsui et al and Thickbroom and Mastaglia were correct in their observations. The spike recorded over the parietal cortex probably has a strong contribution from far-field potentials originating in subcortical sources which are involved in extraocular muscle innervation discharges related to eye movement (as argued by Tsutsui et al). The temporal SP, on the other hand, appears to be derived from extraocular muscle activity (as suggested by Riemslag et al and Thickbroom and Mastaglia). Other cortical or subcortical sources, however, may also contribute to the late presaccadic activity over the temporal and parietal cortex.

Regarding the morphology of the SP, detailed examination of numerous individual perisaccadic recordings from our data set suggests that two or more monophasic peaks, superimposed on a (probably biphasic) slower frequency wave, comprise the late presaccadic activity (Fig. 2). Riemslag et al argued for a biphasic nature of the SP and suggested that the positive phase, occurring after the onset of eye movement, is masked by the following large amplitude EOG artifact. The present data support this argument. High band-pass filtering revealed an apparent biphasic nature of both the temporal and parietal SPs. However, the multiple peak potential which was often apparent in the evoked potential recordings of single saccades could not be clearly demonstrated in the average trace. In summary, we argue that the SP is composed of: (1) high-frequency multipeak activity, (2) lower frequency biphasic waves, best demonstrated with the high-pass filter, and (3) an even lower frequency monophasic wave (including but not necessarily limited to the AP), best recorded with the low-pass filter. Further work is needed to reveal the different cerebral/ocular sources contributing to these potentials.

**Key words:** human evoked potentials, voluntary/spontaneous saccades, cortical/subcortical origin

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References


