A simple method for computer quantification of stage REM eye movement potentials

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Abstract

We describe a simple method for computer quantification of eye movement (EM) potentials during REM sleep. This method can be applied by investigators using either period-amplitude (PA) or Fast Fourier Transform (FFT) spectral EEG analysis without special hardware or computer programming. It provides good correlations with visual ratings of EM in baseline sleep and after administration of GABAergic hypnotics. We present baseline data for both PA and FFT measures for 16 normal subjects, studied for 5 consecutive nights. Both visually rated and computer-measured EM density (EMD) showed high night-to-night correlations across baseline and drug nights and the computer measures detected the EMD suppression that is produced by GABAergic drugs. Measurement of EM in addition to stage REM provides biologically significant information and application of this simple computer method, which does not require pattern recognition algorithms or special hardware, could provide reliable data that can be compared across laboratories.

Descriptors: Computer method, Eye movement density, Trait

Rapid eye movements (EMs) are a salient and easily recorded “phasic” feature of human REM sleep. Although quantification of EM activity is not specifically included in the Rechtschaffen–Kales (1968) scoring manual, many investigators have found it instructive to measure EM potentials as well as stage REM in human sleep studies. EM quantification has usually been performed on ink-written tracings, either with intensity scale ratings (Clark et al., 1999; McPartland, Kupfer, Coble, Spiker, & Matthews, 1978) or by counting the number of epochs in stage REM that contain EM potentials (Feinberg, 1967; Feinberg, Floyd, & March, 1987). Several specialized computer methods for quantifying eye movements have also been described (reviewed in Takahashi & Atsumi, 1997). Almost all EM measurements have been performed on potentials recorded with relatively short time constant (TC; 0.3–0.4 s) polygraph recordings, a notable exception being the study of Takahashi and Atsumi, which used a TC of 3.2 s. We show here that computer measurement of short time constant recordings of EM potentials in visually defined, artifact-free stage epochs of REM provides excellent correlations with visual ratings of eye movement of the sort used by most laboratories. This computer method avoids the need for pattern recognition algorithms or special hardware. It can be immediately applied by investigators using either Fast Fourier Transform (FFT) spectral analysis or period-amplitude (PA) measurement for EEG analysis.

Methods

Our first goal was to determine the frequency bands into which eye movement potentials fall when recorded with a short time constant (0.3 s). Next we examined whether PA or FFT measurement of these potentials in visually defined stage REM epochs yields adequate correlations with a typical method of visual eye movement rating. Correlations of computer with visual ratings were performed for baseline sleep and after the administration of a hypnotic that suppressed eye movement activity. We also examined within-S, across-night correlations of EM measures in baseline sleep and after hypnotic administration to determine whether EM activity is a stable individual trait.

Data Set

Digitized records for these analyses were from a study of the effects of GABAergic hypnotics on the sleep of normal young adults (for preliminary reports, see Feinberg, Maloney, & Campbell, 1995a, 1995b). Participants were 10 men and 6 women ages 19 to 26 years old (mean = 22.07, SD = 2.53). The study consisted of four separate 5-night treatment arms. In one arm, participants received placebo on all 5 nights. In the other three arms, participants received one of three hypnotics on the first 3 nights followed by placebo on the final 2 nights. The drugs were 0.25-mg triazolam, 10-mg zolpidem, and 30-mg temazepam. The minimum washout period between drugs was 4 days. Drugs and placebo were administered orally in identical capsule one-half-hour before bedtime. Each participant completed all four treatment arms. The University of California, Davis Human Subjects Review Committee approved the study, and all participants gave informed consent.
Recording
EEG and EOG were continuously recorded on a Grass 78 poly- 
graph with a TC of 0.3 s. Filter settings were < 0.3 Hz (high pass) 
and 0.1 kHz (low pass). The EM lead (left outer canthus to 
mid-forehead) responded to both vertical and horizontal EMs. EM 
potentials were digitized at 50 Hz and analyzed with PASS PLUS 
(Delta Software, St. Louis, MO). This program can apply FFT and 
PA analysis with both zero-cross and zero first derivative halfwave 
measurement.

Period-Amplitude Analyses
The computer analyses in the original study were performed with 
zero-cross and zero first derivative methods. The algorithms for 
these methods have been presented and their reliability demon-
strated (Feinberg et al., 1978; Feinberg, Fein, & Floyd, 1980b). 
Both PA methods use linear interpolation to enhance frequency 
resolution. For EM measurement, we increased the 5 μV EEG 
smoothing constant to 50 μV to minimize contributions from EEG 
potentials; for a definition of smoothing constant in PA analysis, 
see Feinberg et al., 1978.

Spectral Analysis with FFT
Most FFT parameters (e.g., size of epoch, method of window 
taper, etc.) are specifiable with PASS PLUS. Here we re-analyzed 
the digital data from the original study with FFT using 30-s epochs 
of 5.120 s Welch tapered windows with 2.620 s overlap. This 
yielded 12 windows per 30-s epoch. The power spectrum was 
compressed into eight frequency bands: 0–0.3, 0.3–1, 1–2, 2–3, 
3–4, 4–6, 6–8, 8–25 Hz. The same frequency bands were used for 
the PA analyses. FFT analysis of EM was applied to only a subset 
of the data whereas PA analysis was carried out on all nights as 
part of the original study; for preliminary reports of the drug 
effects, see Feinberg et al., 1995a, 1995b.

Visual Scoring
The EM method we used is applied to epochs that have been 
classified visually as stage REM that are free of body movement 
and other artifacts. Sleep stage scoring was done according to 
activity was performed by counting the number of 2-s segments 
of stage REM that contained EM potentials with amplitude >25 μV. 
These counts provided the criteria for selection of the computer 
measures and were performed without knowledge of the computer 
results. Visual EM density was measured on Nights 2 and 3 of 
baseline placebo and Night 3 of temazepam administration. Eye 
movement density was equal to the number of 2-s segments of 
stage REM rated by the scorer as containing eye movement activ-
ity divided by the total number of 2-s segments of stage REM. 
EMD for the computer measures is FFT power, or with PA analy-
sis, integrated amplitude and time in band with all measures 
expressed per 30-s epoch of stage REM.

Results
We first examined the distribution of EM potentials by frequency 
bond. Figure 1 showed that most of the activity fell into the 
0.3–2 Hz band for both spectral power and period-amplitude mea-
sured integrated amplitude. We then compared the correlations of 
a range of frequencies with the visual ratings of EM density. We 
found that 0.3–2 Hz, which contained most of the spectral power 
and integrated amplitude activity, provided the highest correlations 
with the visual counts, although other frequency ranges sometimes 
(but not consistently) yielded equally high correlations. Figure 2 
shows scattergrams of computer measured eye movement den-
sity for spectral power and integrated amplitude in 0.3–2 Hz 
plotted against visual density ratings on the second baseline night. 
It can be seen that the relationship was roughly linear and the 
correlation coefficients did not depend on outlying points. Figure 3 
shows that the relation of visual to computer measures of eye 
movement density held equally well for the third drug night of 
temazepam administration, when eye movements were signifi-
cantly suppressed by the drug. Several other period amplitude 
measures in 0.3–2 Hz yielded correlations with visual ratings of 
EM density comparable to those for integrated amplitude (.90). 
These included zero-cross curve length (peak-trough amplitude, 
r = .90), zero derivative curve length, and time in band (.89 and 
.82, respectively). These measures are obviously not independent 
of integrated amplitude because they reflect either amplitude or 
incidence components of 0.3–2 Hz potentials.

Table 1 presents the 5-night baseline mean, range, and standard 
deveiation for computer-measured eye movement density as 0.3– 
2 Hz spectral power or period amplitude integrated amplitude, as 
well as the separate amplitude (average sample amplitude) 
and incidence (time in band) elements of integrated amplitude (i.e., 
increment amplitude = average sample amplitude × time in band; 
ctf. Feinberg et al., 1978). To normalize for different REM dur-
ations, data were divided by the number of 30-s REM epochs.

Individual differences in visually scored EMD were relatively 
stable across the two nights on which they were performed (bas-
eline Nights 2 and 3), r = .78, p < .01. Night-to-night agreement for 
these two nights was similar for the spectral and period amplitude 
measures of EMD. Correlation coefficients were also computed 
across the 5 successive baseline nights for integrated amplitude 
and spectral power in 0.3–2 Hz (N1 versus N2, N2 versus N3, 
etc.). For integrated amplitude, the four correlation coefficients 
were .82, .81, .85, and .88; for spectral power, they were .71, .81, 
.79, and .88 (p < .01 for all).

Suppression of eye movement density is a well-known effect of 
GABAergic hypnotics. As part of our original study, which used 
only period amplitude analysis, we performed a repeated measures 

![Figure 1. Percent of spectral power and PA integrated amplitude in 0–25 Hz found in various frequency bands.](image)
ANOVA for 0.3–2 Hz integrated amplitude measure of eye movement density across Nights 1–3 of placebo and the 3 nights of each drug condition. The $F$ for drug treatment effects on EMD was highly significant, $F(3,45) = 8.63, p < .0001$ and post hoc Tukey tests were significant (alpha = .01) for triazolam and temazepam but not zolpidem.

One question that arises regarding the suppression of stage REM eye movements by GABAergic hypnotics is whether the amplitude or the incidence of the eye potentials is reduced. This question can be addressed by period amplitude analysis by examining the separate amplitude and incidence components of the integrated amplitude measure. Average sample amplitude and time in band/30-s epoch for 0.3–2 Hz potentials represent density measures for amplitude and incidence respectively (see above). We compared these measures on the third night of temazepam with the 5-placebo night mean. Temazepam suppressed amplitude and incidence of eye movements by similar extents, reducing amplitude to 87% ($p < .001$) and incidence to 91% ($p < .02$) of their baseline means.

Discussion

These data show that most of the power of EM potentials falls into the 0.3–2 Hz frequency band when recorded with 0.3-s time constant. Although there are lower levels of activity in frequencies up to 8 Hz, including this activity does not improve the correlation of computer measures with visual EM ratings. In 0.3–2 Hz, spectral power and period amplitude measures of integrated amplitude and its incidence and amplitude components correlate well with visual eye movement ratings. Spectral power and integrated amplitude are homologous in that both measures reflect the combined effects of wave amplitudes and incidence. They are well correlated in 0.3–3 Hz EEG (Uchida, Feinberg, March, Atsumi, & Maloney, 1999). We therefore recommend that investigators working with period amplitude methods use integrated amplitude for EM measurement, as this would facilitate comparison of results obtained with the two methods.

Both spectral power and integrated amplitude in 0.3–2 Hz were reasonably stable in baseline sleep, showing substantial and highly significant correlations across successive baseline nights. The internight consistency of computer-measured eye movement found here corroborates early findings in our laboratory with visual EM rating (Feinberg, 1974). Further evidence that eye movement density is a relatively stable individual trait is that participants’ depressed drug levels on the third night of temazepam remained significantly correlated with their baseline means.

![Figure 2](image1.png)

**Figure 2.** Scattergram of visual EM density versus computer measured EM density (0.3–2 Hz integrated amplitude and spectral power) on the second baseline night.

![Figure 3](image2.png)

**Figure 3.** Scattergram of visual EM density versus computer measured EM density (0.3–2 Hz integrated amplitude and spectral power) on the third night of temazepam.
Table 1. Mean Values for PA & FFT Measures of EMD on 5 Consecutive Baseline Nights

<table>
<thead>
<tr>
<th></th>
<th>IAM</th>
<th>ASA</th>
<th>TIB</th>
<th>No. Epochs</th>
<th>POW</th>
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<tr>
<td>S1</td>
<td>120.27</td>
<td>8.55</td>
<td>14.04</td>
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<td>185.97</td>
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<tr>
<td>S2</td>
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<td>16.35</td>
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<td>13.90</td>
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<tr>
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<td>12.86</td>
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</tr>
<tr>
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<td>8.26</td>
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<tr>
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<td>SD</td>
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<td>2.42</td>
<td>30.82</td>
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Number of subjects = 16. Definitions of measures: IAM = integrated amplitude (μV-s), ASA = average sample amplitude (μV), TIB = time in frequency band (s), POW = FFT-measured spectral power (μV²-s). Data for one subject was based on 4 nights, because I might have had severe artifact.

In considering these results, one must remember that polygraphic recording of EM potentials with capacitance coupled (AC) amplifiers provides limited information on the actual direction of the movements or the position of the eyes (cf. Tursky & O’Connell, 1966). These limitations can be overcome with DC or long TC recordings, but these are rarely used. Our use of a single EM channel further limited the information we obtained because it did not distinguish between vertical and horizontal EMs; a rough separation could be achieved with two appropriately configured channels. But no matter how many leads are employed, short time constant EM recording, as Tursky and O’Connell demonstrated, provides only a sampling of the total eye movement activity. Nevertheless, such sampling has provided significant biological information. It has shown that EM density is depressed by conditions that reduce within-sleep arousal level, including prior sleep deprivation and administration of GABAergic hypnotics (cf. Feinberg et al., 1987); conversely, EM density increases across the night (as sleep depth diminishes) and it shows a striking further increase when sleep is extended beyond its normal length (Aserinsky, 1973; Barbato, Barker, Bender, Giesen, & Wehr, 1994; Feinberg, Fein, & Floyd, 1980a), becoming extremely “light”. EM density is also increased in clinical populations, including alcoholic and depressed (Gillin, Duncan, Pettigrew, Frankel, & Snyder, 1979; Gillin et al., 1994) patients, a result that might also reflect higher within-sleep arousal levels.

It is also possible that EMs themselves serve no biological function. They may simply be overt but adventitious expressions of the intense, disinhibited neuronal firing that occurs in many motor (and sensory) systems in REM sleep (Evarts, 1967). Outflow of this motor activity to motor neurons that control limb or truncal movements would cause waking and is inhibited postsynaptically by interneurons originating either locally or in the brain stem (for a review, see Chase & Morales, 1994). We hypothesized that motor neurons controlling EMs are not similarly inhibited simply because eye movements do not cause waking. We suggested that the same reasoning would apply to other small muscles such as middle ear muscle activity (MEMA), which also increases during REM and does not cause waking (Feinberg et al., 1987; Pessah & Roffwarg, 1972).

The EMs of REM sleep, long neglected in favor of measurement of stage REM, are increasingly recognized as important biological variables. The value of the method for quantifying EMs outlined here is that it requires no special programming or hardware. It is less laborious than visual ratings and can be immediately applied by the many investigators already performing spectral or period amplitude analyses of sleep EEG. It is true that many automated scoring systems already detect and measure EMs. However, their algorithms differ and most are unpublished, making it difficult to compare findings obtained with different systems. With proper attention to recording technique, including calibration, EM quantification with the method authored here should be directly comparable across laboratories. Such comparability could more rapidly advance our insight into the biological significance of these striking sleep phenomena.

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