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METHODOLOGY

Removing the heart from the brain: Compensation for the pulse artifact in the photon migration signal

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Abstract

Various factors, including variations in the concentration of hemoglobin, determine changes in the transparency of living tissue to near-infrared light. Hence, optical measures have been proposed as a noninvasive method for investigating regional changes in brain activity. However, the amount of near-infrared light traversing a region of the head is also influenced by the periodic changes in blood pressure that occur during the cardiac cycle (pulse). These large changes may obscure smaller, localized events associated with brain activity. We developed a least-squares regression algorithm for compensating for the artifact introduced by the pulse. This procedure takes into account beat-to-beat variability in heart rate and differences in the shape of the pulse among subjects and among recording conditions.

Descriptors: Photon migration techniques, Photoplethysmography, Regional cerebral blood flow measurement

Traditionally, studies of brain function in normal human subjects have relied on surface measures of electrical potentials (electroencephalogram [EEG] and event-related potentials [ERPs]). These methods possess high temporal (1 ms or less) but limited spatial resolution. In recent years, there has been a substantial interest in methods for investigating the hemodynamic and/or metabolic changes that are presumed to follow the activation of localized brain areas during the performance of various tasks. These methods may in some cases reach a high spatial resolution (a few centimeters or less), although their temporal resolution (several seconds) is clearly inferior to that of electrophysiological measures (Churchland & Sejnowski, 1988). Some of these techniques, such as positron emission tomography (PET) or fast magnetic resonance imaging (fMRI), provide maps of regional changes of metabolism and blood flow or of the concentration of hemoglobin (e.g., Belliveau et al., 1991; Frahm, Merboldt, Hänicke, Kleinschmidt, & Boecker, in press; Raichle, 1994). However, given the complementary nature of the information provided by imaging and electrophysiological methods, it would be very useful to be able to record these two types of measures simultaneously. Unfortunately, fMRI involves high-energy magnetic fields, which preclude the simultaneous recording of electrical potentials, and PET measures cannot be obtained quickly enough for informative comparisons with ERP data. Another approach to the study of the activation of localized brain areas is to measure changes in their optical properties (i.e., absorption and scattering). For instance, because hemoglobin absorbs near-infrared light, changes in the concentration of this substance should alter the transparency of brain tissue to this type of light. Hence, noninvasive optical methods have been proposed as a tool for investigating the functional anatomy of the brain in normal human subjects (Chance, 1989).

Noninvasive Optical Measures in the Study of Brain Function

A simple way of studying changes in the optical properties of the brain involves illuminating points on the surface of the head with near-infrared light and determining the amount of light reaching detectors also located on the head surface a few centimeters away. Living tissues such as those of the head (skin, skull, meninges, gray and white matter, etc.) are highly scattering (Svaasand, Tromberg, Haskel, Tsong-Tseh, & Berns, 1993). In highly scattering media, light travels in spherical waves. Given the random nature of scattering, the light path between a source and a detector can be described as a distribution of paths followed by individual photons. Although in infinite scattering media the average path corresponds to a straight line, if the

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medium is bounded by a flat or convex surface (as it is the case for the head), photons penetrating a point on the surface of the medium will, on average, follow a quasi-semicircular path before reaching another point on the same surface (Maier & Gratton, 1993). For example, light penetrating the head at a particular point and reaching another point on the surface of the head at a distance of 3 cm from the source will have traveled along a semicircular path, reaching an average depth of about 1.5 cm. This prediction was confirmed by phantom studies, which showed that deep absorbing objects can be visualized in this manner, even through bony structures such as the skull (Gratton, Maier, Fabiani, Mantulin, & Gratton, 1994b).

The optical properties of brain tissue are influenced by several factors, including changes in the concentration of metabolically or hemodynamically significant substances and changes in the reflectivity and shape of neurons (see Frostig, 1994). These phenomena produce changes in the scattering and absorption properties of the tissue and, as a consequence, influence the migration of photons through the brain. Preliminary observations and Monte Carlo simulations (see Gratton et al., 1994a) suggest that measures of the attenuation of light (i.e., intensity measures) passing through the head may be influenced by changes in both scattering and absorption properties of the tissue, such as those determined by neuronal activity or changes in the concentration of oxy- and deoxyhemoglobin. For these reasons, changes in the transparency of the tissue have been proposed as an inexpensive and noninvasive method for investigating regional activation of the brain during psychological tasks (Chance, 1989). Reflectivity measures of the exposed cortex of animals indicate that sustained stimulation of an area of the cortex produces changes in the intrinsic coloration of the tissue, which start within 1 s from the beginning of stimulation and reach their peak about 2–3 s later (Grinvald, Lieke, Frostig, Gilbert, & Wiesel, 1986). This intrinsic signal probably comprises several phenomena, including scattering changes due to variations in the refraction properties of neuronal tissue as a function of neuronal activation and absorption changes due to the dilation of small blood vessel that allow the blood to circulate faster and in greater amount through active areas of the cortex (Frostig, 1994). The latter phenomenon is the same that has been proposed to account for the functional signal observed with fMRI (Frahm et al., in press), and PET (Raichle, 1994). Because noninvasive optical measures can be obtained in a quasi-continuous fashion over extended periods of time, are compatible with electrophysiological recordings, and are less expensive than fMRI and PET, they appear to be an attractive addition to these methods.

A problem with this application of optical measures is that observation of the signals produced by regional activation of brain tissue is hindered by other types of signals possessing relatively similar frequency characteristics. One of these signals results from changes in tissue transparency that are time locked to the heartbeat, that is, to the pulse (see Frostig, 1994). Changes in light parameters associated with the pulse have been used for years to investigate functional changes in the cardiovascular system (photoplethysmography, e.g., Jennings & Choi, 1983). Pulse parameters have long been associated with various physiological and psychological variables (e.g., Roy & Sherrington, 1890). Although changes in pulse parameters may in some cases be very informative, they have important limitations. First, pulse parameters can only be measured at successive heartbeats (i.e., the sampling rate is dependent on heart rate). Second, optical measures of pulse parameters are influenced to a large extent by large vessels whose spatial relationships with the cortical areas activated during a certain task may vary from case to case (e.g., Grinvald et al., 1986). For these reasons, pulse parameters are unlikely to provide more than preliminary indications about the dynamic activation of various brain areas during a particular task. However, as indicated by exposed cortex studies, the intrinsic optical signal of the cortex can be very localized and relatively rapid (Grinvald et al., 1986). Therefore, because the purpose of this study is to focus on the dynamics of local functional changes of the optical signal, the large, quasi-periodic fluctuations due to the pulse can be considered as a source of noise. This is particularly problematic because these fluctuations (which we estimate to be as high as 6% of the total amount of light passing through the head) are several times larger than the intrinsic functional signal from the brain tissue (our initial measurements estimate this signal to be less than 2% of the amount of light). Because the pulse signal is unavoidable, we needed a procedure to remove the pulse signal from the records in such a way as to leave the intrinsic optical signal unaltered.

Fortunately, the magnitude of the pulse allowed us to estimate its influence with high precision. One strategy for reaching this goal would be to compute the average pulse waveform and then subtract its influence from the original records. One problem with such an approach is that the amplitude of the pulse may vary from beat to beat. This variation can be accounted for by scaling the average pulse waveform to the size of each single pulse before subtraction. The scaling factor can be estimated with a regression algorithm. Another problem is that the interbeat interval of the heart is variable. Herein, we propose a regression technique that accounts for the beat-to-beat variability of heart rate. In this procedure, heartbeat intervals are expanded to a common, longer time scale before averaging them to compute the average pulse. Then, for each heartbeat, the average pulse waveform is scaled back to the original length of each heartbeat interval. Finally, the rescaled average pulse is regressed with and subtracted from each single heartbeat record. The outcome of this process is a time series reflecting the deviation (in terms of waveshape) of each single pulse from the average pulse. This time series is used as the corrected optical record.

Although several parameters related to the migration of photons through tissue can be measured (see Gratton et al., 1994b), in this report we focus on the intensity (or attenuation) parameter (equivalent to the DC signal reported by Gratton et al., 1994b) because (a) the intensity parameter is easier to measure, requiring less sophisticated instrumentation (i.e., the apparatus needed to measure the time photons take to migrate through the tissue is not needed) and (b) preliminary studies (e.g., Gratton et al., 1994a) have indicated that the intensity parameter is much more sensitive to contamination from the pulse than are other optical parameters.

Method

Assumptions and Procedure

The procedure is based on the following assumptions.

1. Heartbeats (systoles) produce periodic increases in blood pressure (pulse), which in turn, result in periodic increases in the amount of blood flowing through the area being measured.

2. The increase in blood flow produces an increase in the absorption of near-infrared light, which can be measured as a reduction in the amount of light reaching the detector. This reduction will have the same periodicity as the heartbeat.
3. The shape of the pulse, as measured by the periodic changes in the intensity of the light reaching the detector, may vary as a function of the position of the coupling between the source and the detector and the skin, of the location of the optical devices over the head, of the subject, and, in some cases, of experimental conditions. However, when these factors are taken into account, the residual variance in the shape of the pulse signal is small and negligible (at least as a first approximation).
4. In contrast to shape, the wavelength and amplitude of the pulse signal may (and usually will) vary considerably from trial to trial. Wavelength variability is particularly critical and requires a time warping approach (i.e., reduction or expansion to a common time scale) for the computation of the average pulse.
5. The signal-to-noise ratio of the pulse signal is sufficiently high to afford accurate estimates of the timing of each heart systole.
6. The phase delay between the pulse and the functional phenomena studied is random.

On the basis of these assumptions, we propose that the average pulse signal can be computed by (a) recording continuously the amount of light transmitted between the source and the detector, (b) segmenting the continuous records into single-beat periods, (c) time warping the single-beat signal to a longer time scale (in the examples reported herein, we expanded each interbeat interval to 50 s by adding linearly interpolated data points whose numbers depend on the ratio between 50 s and the length of each interbeat interval), and (d) averaging the single beats together. This operation may be conducted independently for each subject, location, recording session, and, if required, experimental condition to account for possible variability in the average pulse.

The deviations between the single-beat signal and the average pulse signal can then be computed by (a) reversing the time warping procedure for each single beat (i.e., compressing the average waveform to the length of each interbeat interval by sampling appropriately distanced data points), (b) regressing the average pulse with the single-beat signal, and (c) subtracting the estimated contribution of the average pulse from the single-beat signal (only the slope, not the intercept, is used for the subtraction). The result is a continuous recording of the amount of light passing through the tissue from which the estimated contribution of the pulse has been removed (or at least attenuated).

A potential problem with this technique is the introduction of discontinuities in the signal at the boundaries between single heartbeats, as determined by fluctuations in the fit of the average pulse to each single beat. To avoid this problem, the average pulse is detrended before the computation of the single-beat regressions. In this way, the first and the last point of the average pulse waveform are set equal to 0 (although intermediate points will be left free to vary). Therefore, the regression algorithm (which does not take into consideration the intercept, only the slope) will never correct the values observed for the first and last data point of each pulse, thus ensuring that the corrected waveform will not show discontinuities between beats. An added advantage of this operation is that the overall shape of the optical parameter waveform across heartbeats will be preserved.

A preliminary step for the procedure is the detection of the beginning of each single heartbeat. To minimize errors due to measurement noise, we chose to base this operation on the smoothed time derivative of the intensity signal. The beginning of each heartbeat cycle is defined as the minimum of this transformed signal within a particular time window following the beginning of the previous heartbeat. In this fashion, the inflection point of the pulse waveform (equivalent to the moment of maximum increase in the light absorption, presumably determined by the systolic pressure wave) is used to define the beginning and end of a pulse cycle. This point of the cycle (rather than the point of maximum or minimum in the intensity wave) was chosen because, being intermediate between the maximum and the minimum, it appeared to be more representative of the average amount of light passing through a particular brain area during each heartbeat cycle and less influenced by outlier values. The time window is selected after visual inspection of the single session data with the intent of accommodating for the apparent variability in the interbeat intervals. Criteria used in the selection of an appropriate time window include (a) the lower limit should be sufficiently high to avoid detecting two points belonging to the same heartbeat and sufficiently low to avoid missing a heartbeat, and (b) the upper limit should be sufficiently low to avoid including two heartbeats in the same epoch and sufficiently high to avoid missing a heartbeat.

Subject and Recording Apparatus

Data were collected from one of us (male, 25 years of age). Infrared light (peak wavelength = 715 nm) produced by a light emitting diode (LED, power = 200 mW) was shone through the head and collected using a 6.4-mm optic fiber. The intensity of the light reaching the fiber was measured using a photomultiplier and digitized at a frequency of 20 Hz, using a specially modified A/D card built by ISS, Inc. (Champaign, IL). The source LED was located 3 cm to the left and 1 cm above the inion, and the detector fiber was located along the midline 1 cm above the inion. Both the source and the detector were inserted in a foam cushion that was held in place by surgical tape wrapped around the subject's head. Surgical tape (with appropriate holes for the source and the detector) was also used to separate the hair so as to increase the amount of light passing through the subject's head. For the same purpose, a drop of petroleum jelly was applied on both the source and the detector. Several layers of black electrical tape were inserted between and around the source and the detector to prevent the detector from collecting light directly from the source (short circuiting the head) or from environmental sources. Given the location of the source and detector, our previous studies with phantoms (Gratton et al., 1994b) suggested that the area of the head traversed by the photons included areas of the skin, skull, meninges, and cortex in the posterior occipital region, close to the occipital pole. In humans, the cortical areas examined are usually associated with visual function.

Task

The study comprised 16 stimulation and 16 control trials. Each trial lasted approximately 30 s, and stimulation and control tri-

als alternated, so that each stimulation trial was immediately followed by a control trial. During the stimulation trials the subject, comfortably sitting in a darkened room, fixated on a computer monitor displaying four vertical grids (visual angle, ca. 3° × 3°; spatial frequency, ca. 3 cycles/degree) arranged on a 2 × 2 matrix. The black and white bars of the top left matrix switched color at a frequency of 1.4 Hz. The other grids remained unmodified. The subject's task was to fixate on the center of the alternating (top left) grid. Recording of the intensity of the light reaching the detector initiated 1–2 s after the beginning of each trial and lasted for 20 s, with data collected at 20 Hz. The control trials were similar, except that the grids were replaced by a stationary display containing columns of alphanumeric characters. The same control display was used for all of the control trials. This task was only used to provide exploratory data on an elementary form of activation of occipital brain areas to study the effects of artifacts on optical data.

Results

We present examples of the application of the technique and formal measurements of the increase in the signal-to-noise ratio obtained with the pulse compensation algorithm. We tested the following basic assumptions.

1. We can obtain a reliable estimate of the moment at which each systole occurs.
2. The wave shape of the pulse (i.e., the sphygmic wave) does not change during a recording block and is independent of the interbeat interval, that is, the shape of the average sphygmic wave is a reliable measure of the pulse effects.
3. Functional changes do not significantly influence the wave shape of the pulse.

Application: Visual Stimulation Versus Control

Figure 1 displays an example of a single trial record, before and after applying the pulse compensation algorithm. A moving average of 5 points (250 ms) was applied to both sets of data to attenuate high-frequency noise. Data are expressed as changes from a baseline value (first 2 s of recording). The compensation procedure resulted in smaller oscillations at the heart rate frequency (slightly above 1 Hz). In the uncorrected data, these oscillations correspond to approximately 6% of the amount of light reaching the detector.

The top panel of Figure 2 shows the average changes during the recording period for the stimulation and control conditions obtained without compensation for the pulse artifact. The scale used for the vertical axis in Figure 2 is four times larger than that used in Figure 1. The scale was increased to accommodate for the expected change in amplitude of the noise, which should be reduced by a factor equivalent to the square root of the number of trials (16). The bottom panel of Figure 2 shows the results of averaging the same data after applying the pulse compensation algorithm. A moving average of 5 points (250 ms) was applied to both sets of data to attenuate high-frequency noise. The effect of stimulation (a 1.5% sustained decrease of the amount of light passing through the occipital head area, developing over a period of more than 5 s) is more evident after application of the pulse compensation procedure (Figure 2).

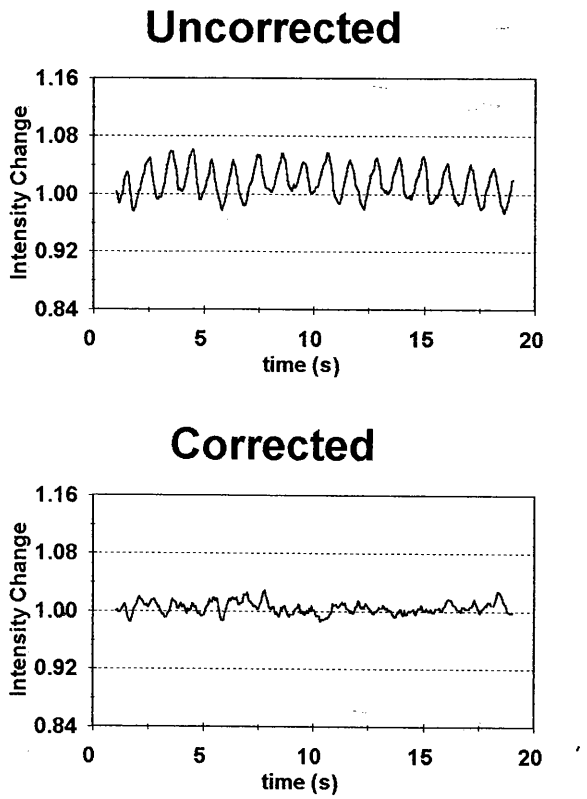

Figure 1. Example of a single trial record, before and after application of the pulse compensation algorithm. A moving average of 5 points (250 ms) was applied to both sets of data to attenuate high-frequency noise. Data are expressed as changes from a baseline value (first 2 s of recording).

Quantification of Increases in the Signal-to-Noise Ratio

The visual impression of a reduction in the signal-to-noise ratio given by the data presented in Figure 2 was quantified by comparing the ratios between the average effect of stimulation and the average amplitude of the noise (i.e., by comparing the signal-to-noise ratios) before and after application of the pulse compensation algorithm. The average signal was estimated by subtracting the mean value of the stimulation condition from that of the control condition for the interval between 5 and 15 s after the onset of the recording epoch. An estimate of the average noise level was obtained by computing the average of the standard deviations of the intensity signal over the same interval for the stimulation and control conditions on each trial. The ratio between these two values was 0.50 for uncorrected data and 0.89 for corrected data. When we consider the reduction in noise level that can be expected by repeating trials 16 times, the signal-to-noise ratios for the averages became 1.93 for the uncorrected data and 3.46 for the corrected data. The critical t score with $df = 15$ (with $\alpha = .05$) is 2.13. Therefore, the correction procedure resulted in an increase in power that, in the example shown (and if the observations had been carried out on different subjects rather than on the same subject), would be sufficient to reveal statistically significant effects that would not be visible otherwise.

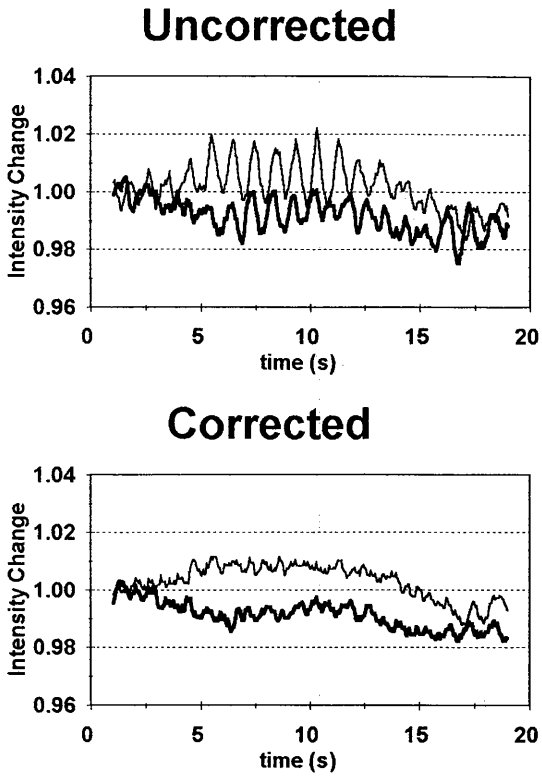

Figure 2. Top: Average changes during stimulation (thick line) and control (thin line) trials for uncorrected data. Bottom: Average changes during stimulation (thick line) and control (thin line) trials for the same data after application of the pulse compensation algorithm. A moving average of 5 points (250 ms) was applied to both sets of data to attenuate high-frequency noise. Data are expressed as changes from a baseline value (first 2 s of recording).

Detection of Heartbeats

A basic assumption of the technique is that it is possible to estimate accurately the time of each heartbeat from changes in the intensity of the light traversing a region of the head that occur at each heartbeat. The algorithm used for detecting each heartbeat is based on identifying the minimum in the smoothed time derivative of the intensity signal within a preselected time window after the previous heartbeat. After visual inspection of the data, a window of 700–900 ms was selected. (For the first heartbeat, an interval between 0 and 900 ms was used.) This window can be considered the allowed range for interbeat intervals. To test the validity of this approach, in one session the electrocardiogram (EKG) was recorded from tin electrodes located on the right and left forearm. The EKG signal was amplified, filtered (range, 1–30 Hz), and digitized (frequency, 128 Hz) over epochs of 20 s, which were synchronous with the optical recording epochs. The R wave of the EKG was detected by visual inspection. Thus, two estimates were obtained for the timing of each heartbeat, one from EKG data and one from optical data. From these data, it was possible to derive estimates of the duration of each interbeat interval with each of the two techniques.

To evaluate the validity of the estimates obtained with the optical data, we computed the means and standard deviations of the difference between the timing of the heartbeats obtained with EKG and obtained with optical data during a stimulation (1-Hz grid reversal) and a control trial. The means were 330 ms in the stimulation trial and 378 ms in the control trial; the standard deviations were 41 and 47 ms, respectively. The mean differences reflect the different time during the cardiac cycle at which the two estimates are obtained and are determined by the time taken by the heart to contract and by the pulse wave to reach the brain (pulse transit time). These differences are irrelevant to the correction itself. The mean differences are higher than the pulse transit time reported in other studies (e.g., Jennings & Choi, 1983); however, there are substantial differences between these studies and the present one in terms both of the methods used to estimate the pulse wave from optical data and of the location at which the measurements are taken. The data reveal a systematic difference between stimulation and control trials, perhaps reflecting differences in vasodilation between the two conditions. Given the preliminary nature of the data, this phenomenon requires further investigation.

The standard deviations of the difference between the EKG and the optical signal reflect trial-to-trial variations in the relative timing of the two estimates. Although timing variations may in fact reflect systematic effects, we assumed that within conditions the actual variations should be small. Therefore, we considered these standard deviations as an upper boundary for estimation of the inaccuracy of the heartbeat detection algorithm. The standard deviations for both stimulation and control trials are below 50 ms, that is, less than one sampling point, which indicates that the procedure for detecting heartbeats from optical data is basically accurate.

An additional analysis was run to provide further confirmation of the validity of the heartbeat-detection algorithm. For each pair of adjacent heartbeats, we computed the difference between the interbeat intervals as obtained from EKG and from optical data. The average of this difference was −2.7 ms (SE = 17.5 ms) for the stimulation trial and −5.3 (SE = 26.7 ms) for the control trial. For both the stimulation and the control trial, the difference was clearly small (much less than the sampling rate) and not significant ($t < 0.2$ in both cases).

Changes of the Average Pulse During a Trial

A further assumption of the procedure is that the wave shape of the pulse (the sphygmic wave) does not change during a recording session. In particular, it is assumed that the wave shape is independent of the interbeat interval, that is, that the wave shape is the same for short and long interbeat intervals. To test this assumption, we compared the average time-warped wave shape for heartbeat intervals longer and shorter than the median (Figure 3). The results suggest some differences between the wave shapes of short and long heartbeats. At some points, one of the curves appears delayed with respect to the other by 4–5% of the interbeat interval. When translated into milliseconds, these differences reach a maximum of about 30–40 ms. Because a sampling rate of 20 Hz (i.e., a sample every 50 ms) was used, the maximum phase difference between the two curves is less than one sampling point. This small difference indicates that the distortion in the pulse wave shape introduced by averaging together fast and slow heartbeat intervals is within measurement error and is therefore negligible (at least as a first approximation). In addition, the two wave shapes are highly correlated (r = .984).

Functional Changes in the Average Pulse

A further question is whether the average pulse wave shape changes as a function of those same experimental variables that

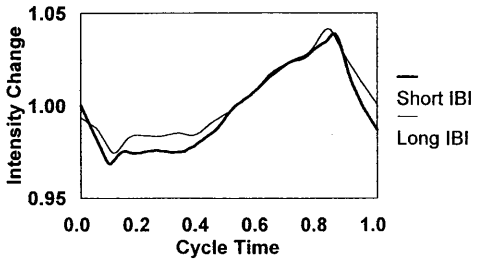

Figure 3. Average time-warped pulse wave shape for heartbeat intervals shorter (thick line) and longer (thin line) than the median. The abscissa indicates the relative timing within the cardiac cycle (0 = systole as detected by the heartbeat detection algorithm, 1 = next systole). The ordinate indicates the intensity change within a cycle.

induce changes in the intrinsic optical signal. If this were the case, by removing the pulse signal we would also reduce or eliminate an important aspect of the signal itself. For this reason, we compared the average pulse wave shape obtained in the stimulation and control trials (Figure 4). (We showed previously that there were systematic differences between these two sets of trials in terms of slow changes in intensity.) The two curves are very similar, and the wave shape of the pulse is the same even though the two conditions differ in the transparency of the occipital region to light (see Figure 2). The two curves are highly correlated ($r = .989$), which suggests that the shape of the pulse signal is largely independent of the functional optical effects. The data presented in Figures 3 and 4 also indicate that the average pulse signal is highly reliable.

Discussion

These various tests indicate that our pulse compensation procedure reduces the size of the pulse artifact on the infrared-light transparency measures. Intrinsic optical changes, presumably induced by visual stimulation, appear more visible after correction. The procedure produces a two-fold increase in the signal-to-noise ratio. Thus, the pulse attenuation procedure significantly increases the power of optical methods for investigating functional changes of brain activity.

Some of the results, in particular those related to the comparison between fast and slow heartbeats, suggest that the technique fails to take into account some minor changes in pulse wave shape. However, the errors associated with these inadequacies of the model apparently do not exceed those that can be expected as a result of measurement error and therefore are negligible. In summary, the various tests support the use of the pulse compensation algorithm in the analysis of optical metabolic measures.

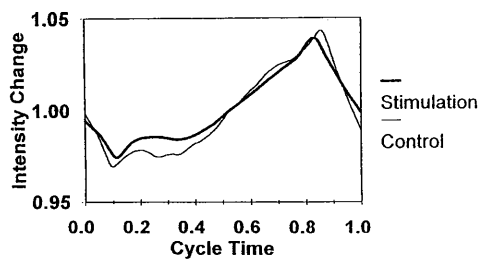

Figure 4. Average time-warped pulse wave shape for stimulation (thick line) and control (thin line) trials. The abscissa indicates the relative timing within the cardiac cycle (0 = systole as detected by the heartbeat detection algorithm, 1 = next systole). The ordinate indicates the intensity change within a cycle.

A problem for this procedure may occur in cases of large heart rate variability such as that associated with various forms of cardiac arrhythmia. Large heart rate variability will make it difficult to choose an appropriate time window between heartbeats for the detection algorithm to work. In addition, the assumption of constancy of the pulse wave shape may be untenable in these cases. Of the various forms of arrhythmia, two appear particularly relevant because of their large incidence in the population: sinus arrhythmia and extrasystolic activity. The effects of these forms of arrhythmia on the pulse attenuation procedure are unclear and require further study. Presumably, an EKG should be recorded simultaneously with optical measures in case of arrhythmia.

Several alternative approaches to the problem of eliminating the pulse artifact can be considered. One approach is to apply to the recordings either a low-pass or a notch filter centered around the heart rate frequency. A difficulty with this approach is that changes in optical parameters due to activation of brain areas may, in principle, have a frequency that is similar to that of the heartbeat (around 0.8–2 Hz). For instance, Grinvald et al. (1986) reported that changes in cortex reflectivity may begin less than 1 s after sustained visual stimulation. Similarly, our observations indicate that changes in the intensity of light traveling through occipital areas of the brain start within the first few seconds after the beginning of stimulation. Although a low-pass filter with a wider band pass (ca. 0–3 Hz) may be used to effectively attenuate at least the higher harmonics of the pulse signal, our recent data (see Gratton et al., 1994a) suggest that the functional optical signal from the brain comprises frequencies that are so fast (i.e., above 3 Hz) as to make this approach impractical. Another approach uses measures obtained at a fixed moment during the heart cycle (e.g., during the diastole). Although this method may have the advantage of reducing the influence of changes in systolic amplitude, it would only allow measures to be taken every second or so (depending on the heart rate of the subject). Because preliminary evidence suggests that changes in light intensity due to the intrinsic optical signal may occur in less than 1 s after stimulation, this method would be too slow.

Our approach estimates the effect of the pulse on optical records on the basis of the recorded data themselves. In this respect, this approach contrasts with other methods of artifact reduction used in other domains, such as procedures used to correct for the ocular artifact in the EEG (e.g., Gratton, Coles, & Donchin, 1983) that correct the artifact on the basis of electro-oculographic (EOG) recordings. An advantage of using an external predictor of the artifact in the correction is that it provides a simple, objective criterion for discriminating between the artifact and the signal of interest. In the case of eye-movement correction methods, vertical and horizontal EOG recordings are supposed to be pure measures of the vertical and horizontal components of the electric fields generated by movements of the eyes or by blinks, practically unaffected by brain electrical activity. In addition, the effects of eye movements on EEG electrodes are supposed to be a fixed proportion of those observed on the EOG electrodes (although this assumption only holds if these

proportions are computed separately for blinks and other eye movements, see Gratton et al., 1983). These assumptions allow us to predict that the shape (i.e., time course) of the artifact will be the same for the external predictor (EOG) and the criterion (EEG). The similarity of the shape of the artifact in the two signals is critical to the application of a correction algorithm based on linear regression. In the present case, however, it is not clear how such an approach could be used. In fact, there is no external signal for which we can reasonably assume that the shape of the pulse waveform will be the same as that obtained from the optical recordings measured at arbitrary locations over the head. For instance, there is no reason to expect that the shape of the pulse at the external carotid will be a good predictor of the shape of the pulse in various locations of the head because the shape of the pulse is known to change from location to location, depending on the speed of propagation of its various components (which in turn is influenced by such factors as blood pressure, viability, elasticity of the arteries, etc.) and on the distance from the heart (see Guyton, 1977). The problem is even worse if the EKG is used as the external predictor.

Our internal-predictor approach has the potential disadvantage of attenuating signals that by their own nature or by accident covary with the pulse. For instance, synchronicity or time locking between stimulations and heartbeat will introduce spurious correlations between the pulse artifact and activation effects and would most likely result in attenuation of the stimulation signal together with the pulse artifact. Fortunately, this attenuation is not likely to occur very often because of variability in heart rate observed in most subjects and can anyway be prevented by using stimulation intervals that are not close to the average heart interbeat interval or that are variable. In addition, over- or undercorrections are possible when the regression procedure fails to account for the appropriate amount of variance. In particular, undercorrections are more likely than overcorrections, because any external source of variance will tend to reduce the correlation between the average pulse and each single pulse and therefore will also reduce the correlation coefficients. For these reasons, this method should be considered as an artifact attenuation method rather than a correction algorithm. Possible improvements in the present technique may include the use of statistical procedures with higher validity and robustness than those used in the present study, such as maximum likelihood (rather than least squares) regression methods, detection and elimination of outliers, and so forth. However, the various tests reported in this paper suggest that the simple methodology used here is sufficient to attenuate considerably the influence of the pulse and to reveal fine changes in optical parameters.

One of the assumptions of the correction method is that the pulse signal is superimposed on the signal of interest (i.e., changes in optical properties in areas of the cortex reflecting local activation) but that it is not contributing to this signal. Some tests of this assumption have been presented, showing its validity as a first approximation. However, this assumption is likely to be only partially correct. Changes in the amplitude of the pulse artifact at a particular location may be expected if phenomena of local vasodilation or vasoconstriction are triggered by substances produced as a result of neural activity. Grinvald et al. (1986) reported changes in the diameter of relatively large blood vessels whose path intersected active areas of the cortex. Although the influence of these phenomena on the pulse measures obtained with noninvasive optical methods remains to be demonstrated, the compensation algorithm probably will reduce eventual pulse changes resulting from this type of mechanism. However, the benefits obtained by compensating for the pulse artifact largely outweigh the costs arising from the elimination of functionally meaningful pulse changes. Separation of the intrinsic optical signal in the cortex from pulse fluctuation is useful because (a) the anatomical relationship between cortical areas of interest and blood vessels is often unpredictable and (b) the effects of heartbeat on optical parameters may be completely different (in terms of direction and pattern) from those determined by the optical intrinsic signal. However, the procedure described in this paper could be conceptualized as a method for separating two components of the optical signal that can be later analyzed individually: (a) the quasi-rhythmic oscillations associated with the pulse and (b) the phasic variations superimposed on this background rhythm, reflecting deviations from fundamental patterns of oscillations. Some of the tests reported in the present paper can be viewed as separate analyses of these two components of the optical signal (as, for instance, the comparisons between stimulation and control conditions carried out on the corrected waveforms and on the average pulse waveforms).

In our algorithm, we chose to use the inflection point associated with the moment of largest reduction in light during a pulse as the anchoring point for the correction. A consequence of this choice, and of the use of a detrending algorithm prior to correction, is that the corrected and the uncorrected signal intersect at this point on each heartbeat. This set of operations preserves the slow components of the signal. The selection of the inflection point was based on the argument that this point may be more representative of the average light intensity during a heartbeat cycle than may other points, such as the minimum or the maximum. This point is bound to show values of light intensity that are intermediate between the minimum and maximum intensity observed during each pulse cycle, which is consistent with a model assuming that the average value across a pulse cycle represents a valid estimate of the true average light intensity during the pulse cycle, once the rhythmic effects of the pulse are removed. Alternative models may assume that the diastolic or systolic values (corresponding, respectively, to the maximum and minimum points of the cycle) are better estimates of the true average. For instance, we could assume that heart systoles cause an increment in the amount of blood in a certain area over and above what would be present otherwise (in this case, the diastolic point, represented by the maximum point within a cycle, would be more representative of the optical conditions once the effects of the pulse were removed). Alternatively, during the diastole, blood will be pumped out of the measured area (in this case, the diastolic point would not be representative because blood is actively removed during this phase). Which of these models is more valid and yields more informative results is a matter for future research. However, the compensation procedure described in this paper can be applied to all of these models by merely changing the point in the pulse cycle used for anchoring.

The results reported in Figure 2 suggest a sustained decrease with respect to control conditions in the amount of light passing through occipital areas of the head during visual stimulation. It is tempting to attribute these changes to slow, regional hemodynamic changes (such as increases in blood flow) caused by visual stimulation. Similar results (although with a lower temporal resolution) have been reported by Frahm et al. (in press), who used fMRI, and by Kato, Kamei, Takashima, and Ozaki (1993), who used optical recordings. However, given the limited

scope of the present study, the methods used do not allow us to determine whether the observed changes are regional or whether they are due to some systemic change in cardiovascular activity or to other factors or if they are reliable at all. In addition to the use of a larger sample size, reaching functional conclusions from these data requires adequate control techniques, which may include mapping the functional changes across the surface of the head and/or the use of a control condition more similar to the stimulation one.

In our example, changes in optical parameters were quantified as proportional variations with respect to a prestimulus baseline period. An advantage of this relative approach is that it allows investigators to compare effects of stimulation under different recording conditions, such as those obtained when recordings are made at several scalp locations or from different subjects. Thus, relative-change data can be used to build activation maps of cortical areas (see Corballis, Gratton, Cho, Fabiani, & Hood, 1994). However, this approach does not permit an absolute quantification of parameters such as the concentration of oxy- and deoxyhemoglobin. Several investigators have attempted to quantify changes in these parameters as a function of stimulation on the basis of noninvasive optical recordings (e.g., Kato et al., 1993). A problem with this approach is that most quantification algorithms assume that the head can be modeled as a homogenous medium. Monte Carlo simulations (reported by Gratton et al., 1994a) suggest that these quantification algorithms may not be applicable when more realistic models of the head are used. A systematic quantification procedure, able to produce a three-dimensional reconstruction of parameters such as the concentration of oxy- and deoxyhemoglobin on the basis of surface optical recordings still needs to be developed.

The data presented in this and other studies lend some credibility to the claim that studies of changes of the optical properties of areas of the head may provide useful information about regional changes associated with psychological functions. Measurement of the transparency of various areas of the head to near-infrared light is quite inexpensive and noninvasive and can, in principle, be combined with electrophysiological measures, as was done here by the simultaneous recording of optical parameters and EKG. The temporal resolution of the technique is excellent, only limited by the speed of the functional changes. The combination of these factors makes the recording of optical parameters a promising new tool for the study of brain function. Compensation for the pulse artifact using procedures such as the one described here results in significant reductions of the noise in optical measures.

REFERENCES

Belliveau, J. W., Kennedy, D. N., McKinstry, R. C., Buchbinder, B. R., Weisskoff, R. M., Cohen, M. S., Vevea, J. M., Brady, T. J., & Rosen, B. R. (1991). Functional mapping of the human visual cortex by magnetic resonance imaging. *Science, 254*, 716–719.

Chance, B. (Ed.). (1989). *Photon migration in tissues*. New York: Plenum.

Churchland, P. S., & Sejnowski, T. J. (1988). Perspectives in cognitive neuroscience. *Science, 242*, 741–745.

Corballis, P. M., Gratton, G., Cho, E., Fabiani, M., & Hood, D. C. (1994). *Functional maps of the human occipital cortex based on noninvasive optical recordings. Psychophysiology, 31*(Suppl. 1), S36.

Frahm, J., Merboldt, K.-D., Hänicke, W., Kleinschmidt, A., & Boecker, H. (in press). Brain or vein—Oxygenation or flow? On signal physiology in functional MRI of human brain activation. *NMR in Biomedicine*.

Frostig, R. D. (1994). What does in vivo optical imaging tell us about the primary visual cortex in primates? In A. Peters & K. S. Rockland (Eds.), *Cerebral cortex* (pp. 331–358). New York: Plenum.

Gratton, G., Coles, M. G. H., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology, 55*, 468–484.

Gratton, G., Fabiani, M., Friedman, D., Franceschini, M. A., Fantini, S., Corballis, P. M., & Gratton, E. (1994a). *Rapid changes of optical parameters in the human brain during a tapping task*. Manuscript submitted for publication.

Gratton, G., Maier, J. S., Fabiani, M., Mantulin, W. W., & Gratton, E. (1994b). Feasibility of intracranial near-infrared optical scanning. *Psychophysiology, 31*, 211–215.

Grinvald, A., Lieke, E., Frostig, R. D., Gilbert, C. D., & Wiesel, T. N. (1986). Functional architecture of cortex revealed by optical imaging of intrinsic signals. *Nature, 324*, 361–364.

Guyton, A. G. (1977). *Textbook of medical physiology* (Italian Edition). Padova, Italy: Piccin.

Jennings, J. R., & Choi, S. (1983). An arterial to peripheral pulse wave velocity measure. *Psychophysiology, 20*, 410–418.

Kato, T., Kamei, A., Takashima, S., & Ozaki, T. (1993). Human visual cortical function during photic stimulation monitored by means of near-infrared spectroscopy. *Journal of Cerebral Blood Flow and Metabolism, 13*, 516–520.

Maier, J. S., & Gratton, E. (1993). Frequency-domain methods in optical tomography: Detection of localized absorbers and a backscattering reconstruction schema. *SPIE Proceedings, 1888*, 420–427.

Raichle, M. E. (1994). Visualizing the mind. *Scientific American, April*, 58–64.

Roy, C. S., & Sherrington, C. S. (1890). On the regulation of the blood supply of the brain. *Journal of Physiology, 11*, 85–108.

Svaasand, L. O., Tromberg, B. J., Haskel, R. C., Tsong-Tseh, T., & Berns, M. W. (1993). Tissue characterization and imaging using photon density waves. *Optical Engineering, 32*, 258–266.

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