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Rapid Changes of Optical Parameters in the Human Brain During a Tapping Task

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Abstract

■ Measures of parameters of the migration of near-infrared photons through the head (attenuation, or intensity, and time-of-flight, or delay) have been proposed as a way of assessing noninvasively and in a quasicontinuous fashion changes in the scattering and absorption properties of brain tissue. These, in turn, may reflect functional changes associated with behavioral tasks. To test this hypothesis, we measured changes of photon migration parameters from scalp locations proximal to the motor cortex from four human subjects, tapping at a rate of 0.8 Hz with their left or right hand, or with their left or right foot. Tapping produced both slow effects (requiring several seconds) and fast effects (tracking the tapping frequency). Slow effects were characterized by increase and delay of the light passing through the hemisphere contralateral to the tapping hand. Fast effects consisted of changes in the light delay during hand tapping. Monte Carlo simulations based on layer models of the brain indicated that fast effects are consistent with changes in deep layers of the head (presumably in the cortex), and that slow effects are consistent with either a shift of absorbing material toward deeper layers or a reduction in scattering. These results suggest that optical parameters can monitor rapid changes of brain activity, matching the contralateral organization of the motor cortex. ■

INTRODUCTION

Noninvasive measures of human brain activity are an important source of data in cognitive neuroscience. Presently, most data are derived from two major groups of techniques: Those investigating changes of the electromagnetic fields produced by the brain (EEG, ERPs, and MEG), and those investigating the accumulation or variation in concentration of marker substances associated with brain metabolism or hemodynamics (PET, SPECT, and fMRI) (Churchland & Sejnowski, 1988). This paper reports a preliminary study on a new approach for studying brain function, based on changes in the optical properties of the brain. In particular, the dependent variables examined indicate the effects of brain tissue on photon migration (both in terms of the attenuation of the light by the brain tissue—*intensity*—and of the time required by the light to pass through the tissue—photons' time-of-flight or *delay*) (see Alper, 1993; Benaron & Stevenson, 1993).

Changes in these parameters are determined, albeit in a complex manner, by changes in the absorption and scattering properties of the head itself (Chance, 1989). Changes in the absorption properties of the brain may reflect changes in the concentration of particular substances, such as oxy- and deoxyhemoglobin, cytochromes, and various pigments. Which substances are targeted will depend on the wavelength of the light. Changes in scattering may also be determined by changes in the concentration of metabolically significant substances, and/or by changes in the reflective characteristics and shape of the membranes of neurons and other brain cells (Frostig, 1994). It is conceivable that the latter changes may reflect the movement of ions that

accompany the normal functioning of the neurons. Therefore, procedures for studying the parameters of photon migration through the brain may become powerful tools in the investigation of brain activity. The purpose of the present study is to determine the sensitivity of these measures to functional changes, as well as to provide initial information on the temporal and spatial resolution of optical methods.

Measurement of photon migration through brain tissue involves illuminating a point on the surface of the head, and determining the intensity and delay of near-infrared light reaching a detector also placed on the head surface at a distance of a few centimeters from the source. Strongly scattering media, such as brain and bone tissue, diffuse light randomly. Previous research shows that, under these conditions, the region of the head relevant to the measurement is a crescent-shaped volume with maximum thickness of up to 1 cm and maximum penetration equal to approximately half the distance between the source and the detector (Gratton, Maier, Fabiani, Mantulin, & Gratton, 1994).

Measuring photon-migration parameters is safe, since very small amounts of nonionizing radiation are used. The recording apparatus is inexpensive (less than 30,000 dollars) and unobtrusive. Measurements can be taken repeatedly in a normally behaving person, over an extended period of time. Intensity measurements can be taken quickly (100 or more times per second). Furthermore, Gratton et al. (1990) showed that it is possible to measure the photon's average time-of-flight, or delay, at the same rate, by using light whose amplitude is modulated at radiofrequencies. In a previous study (Gratton et al., 1994), we showed that frequency-domain photon-migration measures are sensitive to the presence of absorbing objects inside the skull of an animal. Thus, this technique appears suitable for studying noninvasively the dynamics of regional brain activity in humans.

The application of photon migration methods to the study of brain function requires answers to a number of preliminary questions. First, we need to determine whether surface measures are indeed capable of detecting changes in the optical parameters of brain tissue that occur during the performance of a tapping task. Second, we need to derive at least an initial characterization of the pattern of change in the optical signal to delineate the range of phenomena that can be studied with photon migration methods. Third, we need to provide a framework for the interpretation of the results within the context of biophysical models of the optical properties of the head. In this paper we attempt to provide initial answers to these questions by presenting data obtained during a behavioral task (tapping) and with Monte Carlo simulations of the effects of variations of absorption and scattering in different layers of the head.

The choice of a tapping task was based on several factors. First, the brain areas involved in this task (motor areas of the hemisphere contralateral to the tapping limb) are relatively extended and close to the surface of the head. This maximizes the likelihood of observing a signal. Second, by requiring tapping with either the left or right hand or the left or right foot, it is possible to manipulate the area of the brain involved (since the motor system is crossed and hand and foot are differentially represented on the motor strip). Third, by taking measures from sites ipsilateral and contralateral to the tapping limb, it is possible to control for the influence of nonspecific factors (such as changes in heart rate, respiration patterns, or generalized body movements) on the optical parameters, and to obtain some initial clues as to whether the changes observed are regional or systemic. A similar approach has been taken in studies using fMRI (Frahm, Merboldt, Hänicke, Kleinschmidt, & Boecker, 1995) and PET scans (see LaBerge, 1990), and is common practice in the study of human motor potentials (see Coles, 1989). Fourth, the repetitive nature of the task allowed for measurements to be taken repeatedly and very quickly (optical parameters were sampled at 12.5 Hz). Finally, the tapping frequency used (0.8 Hz) provided an initial test of the temporal dynamics of the phenomenon under study (i.e., whether or not the measurements could track the tapping frequency).

The Monte Carlo simulations were designed to allow us to derive a set of predictions on the effects of changes in the absorption and scattering properties of the head on the optical parameters (i.e., intensity and delay). These simulations were based on the assumption that a region of the head can be modeled by a set of layers corresponding to the skin, skull, cortex, etc., and that changes in absorption or scattering are localized to one layer. Layer models of the head are commonly used in the analysis of surface-recorded electrical brain activity (e.g., Nunez, 1981). This arrangement allowed us to test simplified models of the physiological changes occurring in the brain during the tapping task. The results of these simulations are intended to provide a framework for the interpretation of the effects observed during the tapping task.

RESULTS

Tapping Experiment

We performed two types of analyses on the data collected during the tapping task: *time-domain analyses,* evaluating changes in photon migration parameters during each trial, and *frequency-domain analyses,* evaluating the ability of the physiological system under study to track the tapping frequency (0.8 Hz). In each case, differences between the data obtained when the subject was tapping with the limb contralateral and ipsilateral to the light source were considered as indices of functional changes in physiological activity. Since previous studies based on fMRI (Kim et al., 1993) and PET (Remy, Zilbovicius, Leroy-Willig, Syrota, & Samson, 1994) have indicated differences in the extent to which each hemisphere is

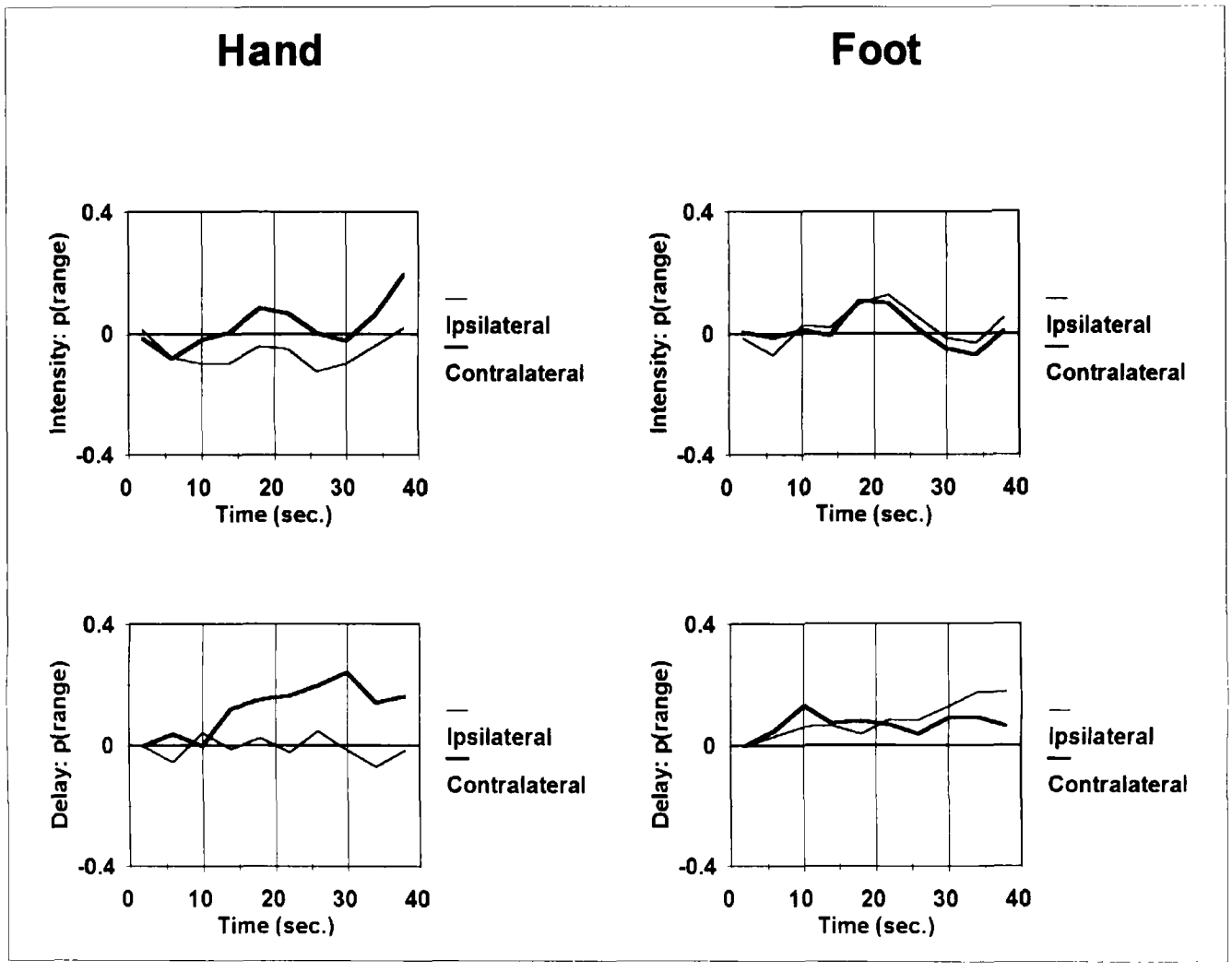

Figure 1. Time course of the photon migration parameters recorded while tapping with the limb contralateral and ipsilateral to the source, pooled across right and left recordings. Data were range-corrected and averaged across trials and subjects. Tapping occurred between sec 10 and 30. The values are reported as changes from a baseline value (sec 0–4). Thick lines represent recordings contralateral to the tapping limb; thin lines represent recordings ipsilateral to the tapping limb. P(range) is equal to proportion of range for each subject.

involved in contralateral and ipsilateral movements, the data obtained from left and right recordings were also analyzed separately, and recording side was entered as a separate factor in the analyses of variance (ANOVAs).

Time-Domain Analyses

Figure 1 depicts average changes in light intensity and delay obtained from sources contralateral and ipsilateral to the tapping hand and foot, pooled across right and left recordings. Figure 2 shows the average *differences* between contralateral and ipsilateral hand and foot tapping, separately for right and left recordings, for both the intensity and the delay parameters. The data are computed as averages of 4-sec periods. The average values over the first 4 sec of recording were used as baseline. For the intensity measure, the values are expressed as proportional variation from baseline. For the delay data, the values are expressed as time delay with respect to the baseline value. Since subjects varied by a factor of more than 10 in the size of the effects, the data were range normalized for each subject before the analysis. This was accomplished by determining the maximum and minimum values for each subject (across all conditions), computing the difference between these two values (i.e., computing the range of variability for each subject) and dividing the value observed for each data point for each subject by the range obtained for that subject. Thus, the effects visible in Figure 1 cannot exceed 1.

Figures 1 and 2 reveal consistent differences between contralateral and ipsilateral recordings during hand tapping for both the intensity and the delay (i.e., time-of-flight) parameters. The statistical analysis was performed on the basis of five 8-sec intervals (respectively, sec 0–8, 8–16, 16–24, 24–32, and 32–40). Note that on the basis of previous fMRI observations (Frahm et al., 1995), it was expected that the effects of tapping would be noticeable

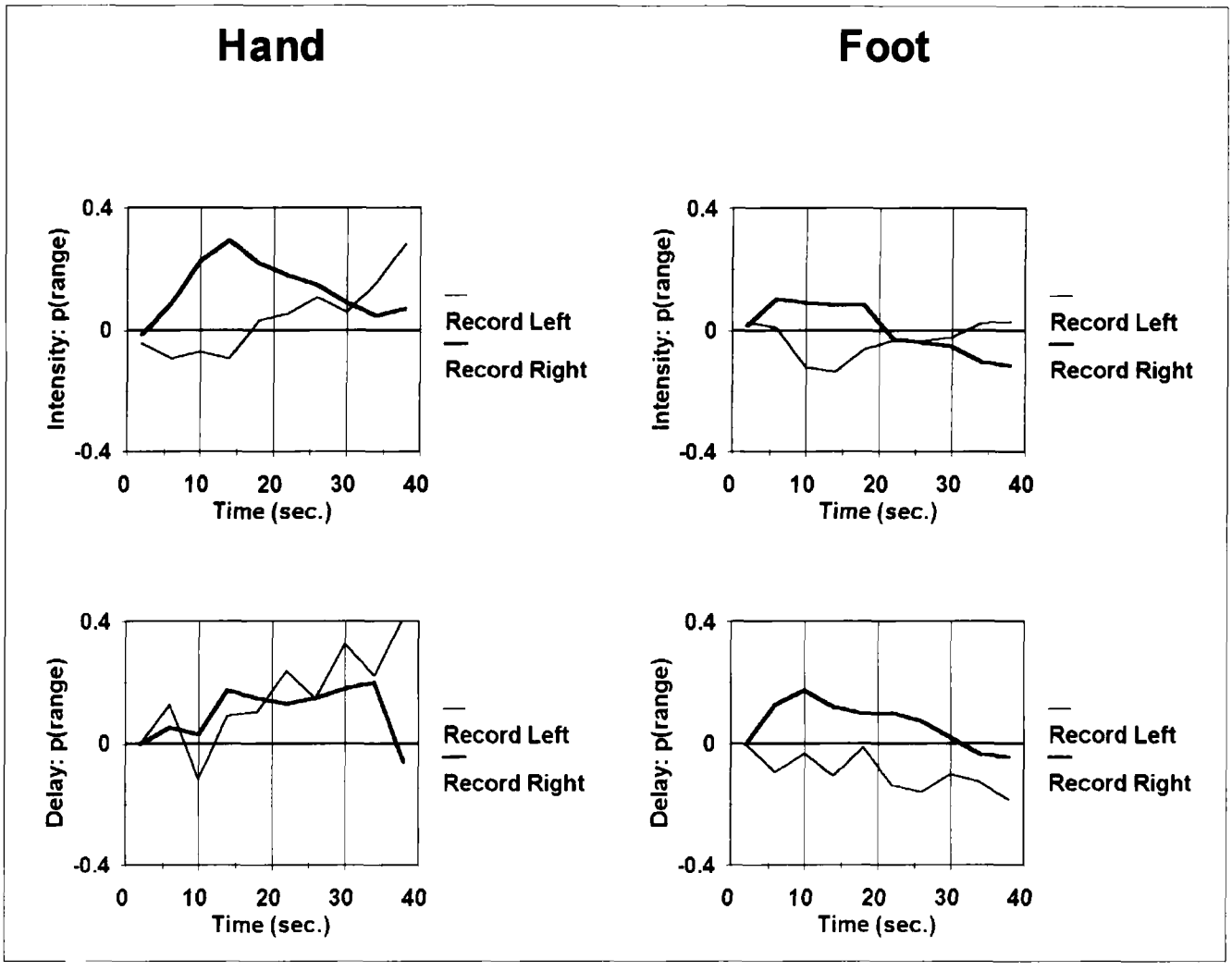

Figure 2. Range-corrected differences between recordings from sites contralateral and ipsilateral to the tapping limb. Tapping occurred between sec 10 and 30. Positive values indicate larger values on the contralateral side, negative values indicate larger values on the ipsilateral side. Thick lines refer to data recorded from right locations; thin lines refer to data recorded from left locations. P(range) is equal to proportion of range for each subject.

over intervals 2 to 4, since subjects were tapping between sec 10 and sec 30. Separate ANOVAs were performed for hand and foot tapping conditions, and for the intensity and delay parameters. Factors included *recording side* (left vs. right), *tapping side* (contralateral vs. ipsilateral), and *interval*. In the case of hand tapping, tapping side produced significant effects both on the intensity and on the delay parameters [respectively, $F(1,3) = 20.81, p < 0.05$, and $F(1,3) = 55.08, p < 0.01$], indicating that more photons reached the detector on the contralateral than on the ipsilateral side, although they also took longer on average to travel through the head. In addition, analysis of the recording side × tapping side × interval interaction suggested a trend for effects to be larger on the right side, at least during the earlier period of tapping, although these effects did not reach significance for either intensity [$F(4,12) = 2.58$, $p < 0.10$] or delay [$F(4,12) = 2.95, p < 0.10$]. For foot tapping, there were no significant effects. However, a significant bilateral effect of foot tapping on intensity emerged when the analysis was restricted to the first three recording intervals [$F(2,6) = 5.13, p < 0.05$].

Frequency Domain Analyses

Differences between the relative amplitude spectra for contralateral and ipsilateral recordings of the photon migration parameters are shown in Figure 3, separately for hand and foot tapping. The spectra were derived for the tapping period (sec 10 to sec 30 of each trial) and were pooled over 0.4-Hz bins. The delay spectrum for hand tapping reveals peaks of activity on the side *contralateral* to the movement around 0.8 and 3.2 Hz (recall that the subject was asked to tap at 0.8 Hz, so these are, respectively, the tapping frequency and its second harmonic). The effects are not evident for the other spectra.

It was hypothesized that given the crossed organiza-

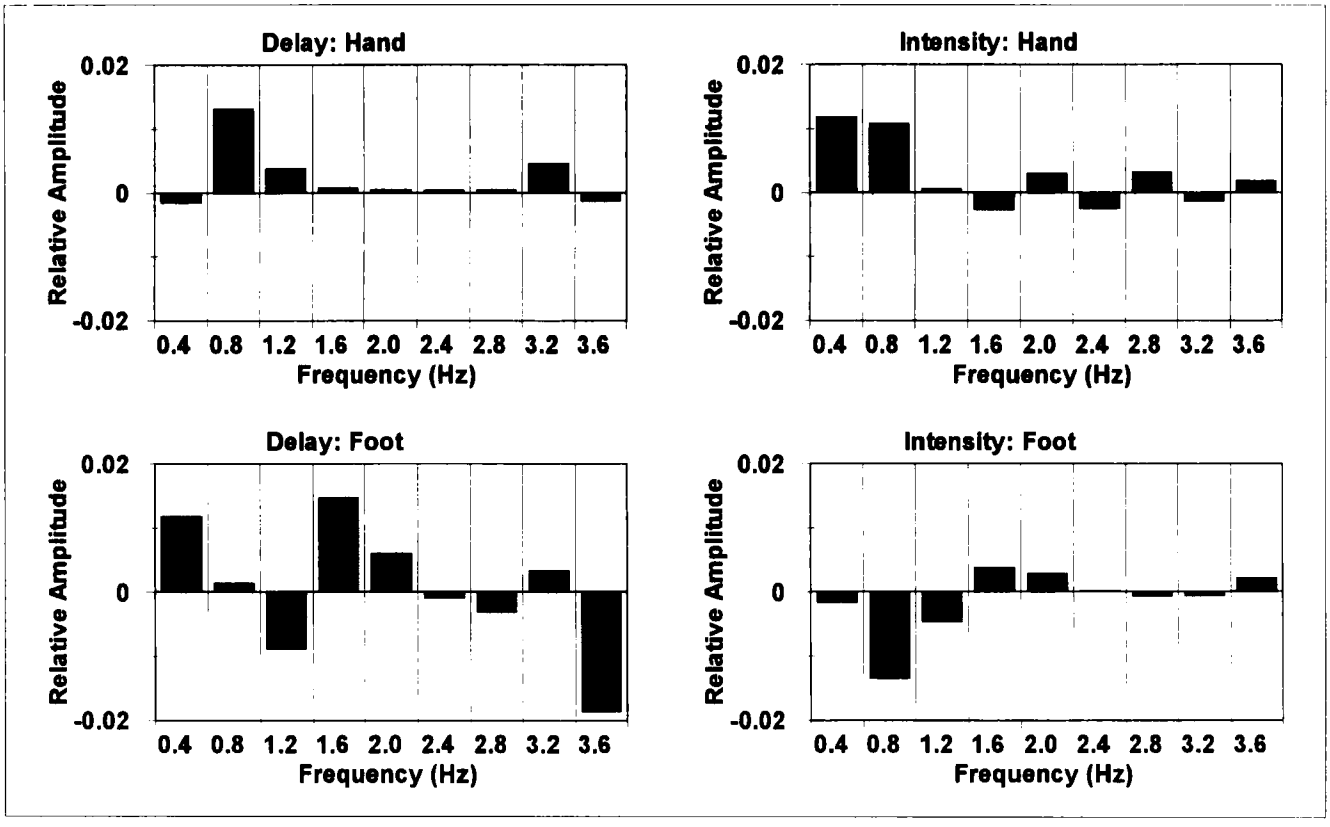

Figure 3. Differences between relative amplitude spectra for recordings contralateral and ipsilateral to the movement, obtained during the tapping period and pooled over 0.4-Hz bins. Positive values indicate greater activity contralateral to the movement side; negative values indicate greater activity ipsilateral to the movement side.

tion of the motor system, we should observe increased activity on the side contralateral to the tapping limb, especially for hand movements. Therefore, one-tailed t tests were performed for each frequency by testing the difference between the relative power on the side contralateral and ipsilateral to the tapping limb. The significant results ($p < 0.025$) are reported in Figure 4. They indicate that for the delay parameters, significant t values were centered around the tapping frequency and its harmonics. This was particularly evident for hand tapping, and less so for foot tapping, where significant effects were obtained at several other frequencies. No clear pattern emerged for the intensity parameter. Note, however, that since a large number of t tests were performed, it is possible that some of the significant results might have been due to chance (α error). Therefore, a second analysis was performed: For each subject we integrated the relative amplitude over a frequency band (0.6–1.0 Hz) centered on the tapping frequency, separately for hand and foot tapping, left and right recordings, and for contralateral and ipsilateral movements. This analysis was performed for each of four 10-sec intervals (sec 0–10, 10–20, 20–30, and 30–40). Note that the first period, before tapping started, could be considered as baseline. Therefore, the effects of tapping were computed as proportional changes in amplitude at the tapping frequency during the tapping periods (average of the second and third intervals) with respect to this baseline. An advantage of this procedure is that it allowed us to evaluate whether differences between the contralateral and ipsilateral side were due to an increase in activity on the contralateral side or to a decrease in activity on the ipsilateral side.[1] The average effects are shown in Figure 5.

The results of this analysis were submitted to separate ANOVAs for hand and foot tapping and for the delay and intensity parameters. The ANOVAs included as factors *recording side* (left vs. right), and *tapping side* (contralateral vs. ipsilateral). The ANOVA on the delay parameter for hand tapping revealed a significant effect of tapping side, with greater activity when the subjects were tapping with the contralateral hand than when they were tapping with the ipsilateral hand [$F(1,3) = 14.89, p < 0.05$). This effect was most evident on the right side, although the recording side by tapping side interaction failed to reach significance [$F(1,3) = 6.20, p < 0.10$). To determine whether the lateralization effect was due to an increase in activity during contralateral movements or to a decrease in activity during ipsilateral movements, separate one-tailed paired t tests were performed for each tapping side, comparing the period of tapping with the baseline period. These analyses revealed a significant increase on the contralateral side [$t(3) = 2.39, p < 0.05$] and a non-significant decrease on the ipsilateral side

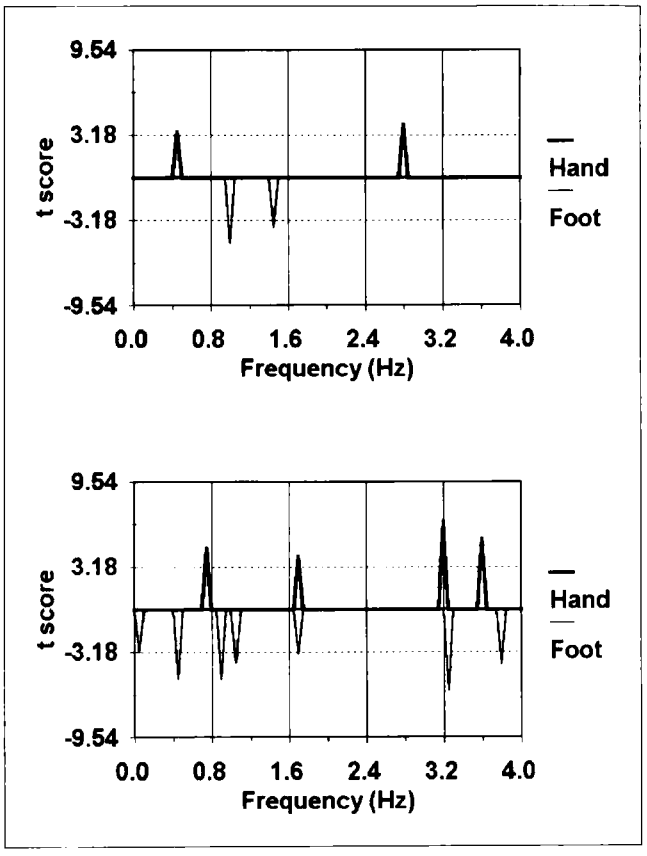

Figure 4. Significant t values ($p < 0.025$, one-tailed) obtained by comparing the amplitude contralateral and ipsilateral to the tapping limb for each frequency (top: intensity; bottom: delay). Upward deflections refer to hand tapping and downward deflections to foot tapping. Only values for frequencies in which activity was significantly greater on the contralateral side than on the ipsilateral side are reported.

[$t(3) = -2.20$, $p < 0.10$]. Thus, although the data are consistent with the hypothesis that tapping produced an increase in activity in the hemisphere contralateral to the tapping hand tracking the tapping frequency, an ipsilateral decrease may also contribute to the lateralization effects. No significant effects emerged from the other ANOVAs.

Monte Carlo Simulations

The purpose of the Monte Carlo simulations was to provide a frame of reference for the interpretation of the changes in photon migration parameters observed during the tapping task. In particular, we focused on five physiological "scenarios" that could account for functional changes in optical parameters: (*a*) increase of absorption in a particular layer (an effect of this type may be due to an increase in cortical blood flow), (*b*) movement of an absorbing substance from more superficial to deeper layers (an effect of this type may reflect movement of blood from the arachnoid and pia mater to the cortex), (*c*) increase in scattering in a particular layer (an effect of this type may be due to the accumulation of a scattering substance or to changes in the shape and/or reflectivity of neurons leading to an increase in the scattering properties of the tissue), (*d*) reduction of scattering in a particular layer (this may be due to changes in the opposite direction to those hypothesized for increases in scattering), and (*e*) increases of both scattering and absorption in a particular layer (this may be due to a combination of the effects hypothesized for scenarios *a* and *c*).[2] These physiological scenarios were evaluated by comparing the intensity and delay effects obtained from simulations carried out using layer models of the head, in which the depth of an absorbing or a scattering layer was varied systematically.

Several models of the head were used: In one model the scattering and absorption properties were assumed to be constant across the head (which was approximated by a semi-infinite medium). This was used as a baseline condition. In the other models, the absorbing or scattering coefficients were increased or reduced in one layer (1 cm thick) with respect to the baseline model. This was achieved by multiplying or dividing the scattering or the absorption coefficient for one layer by a factor of 2.[3] The depth of the layer with changed scattering or absorption properties varied in the different models from 0-1 up to 4-5 cm from the surface of the medium, in steps of 1 cm. For each model, the trajectory and final outcome of each photon were then calculated for a large number of photons (3×10^7) according to a random walk behavior (see Methods section for more details).

The rationale for the choice of these models is to represent conditions before (baseline model) and during tapping (the other models). For scenarios *a*, *c*, *d*, and *e*, differences between models with changed optical properties with respect to the baseline model were intended to represent hypothetical effects on photon migration parameters of changes in scattering and absorption in a head layer, such as the cortex. For scenario *b*, the movement of an absorbing substance into deeper layers is simulated by the difference between conditions in which the absorbing layer is deep with respect to conditions in which it is superficial.

Note that even though large, the number of photons used in each simulation is still very small when compared to real conditions. For this reason, we decided to test relatively large changes in scattering and absorption coefficients. In addition, the models used are obviously extreme simplifications of the complexities associated with brain anatomy and physiology. Hence, the results of the simulations cannot be used to make quantitative statements, but only to form initial predictions about the relative effects of changes in scattering and absorption on photon migration parameters.

The results of the simulations are presented in Figure 6. The validity of the models should be judged on the basis of their ability to yield patterns of effects that are

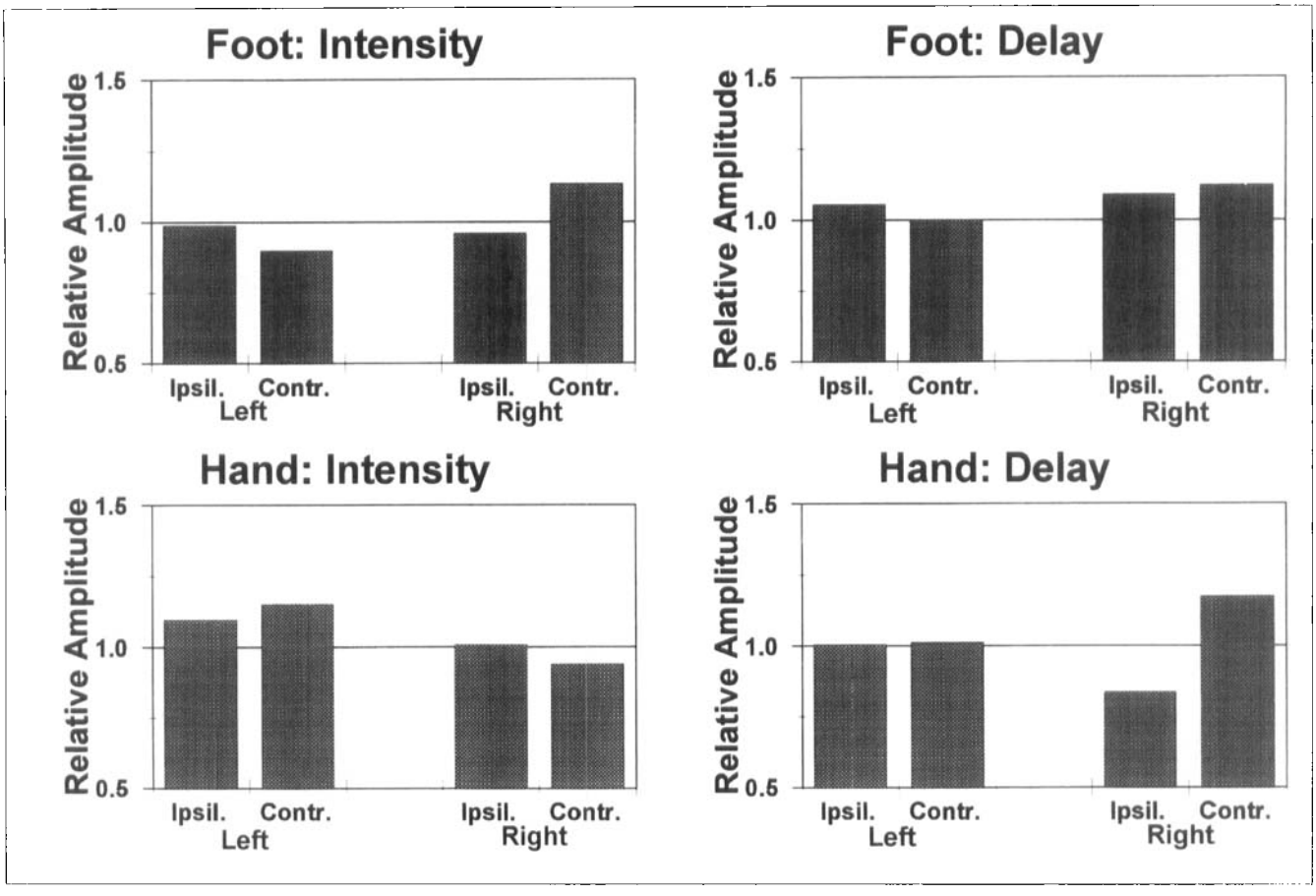

Figure 5. Average ratio between the amplitude at the tapping frequency measured during the tapping task and during the baseline period. Data were pooled over a 0.6–1.0 Hz frequency band separately for hand (bottom) and foot (top) tapping, left and right recording sites, and contralateral and ipsilateral movements.

consistent with the observed data. Note that the results of the study can be summarized in the following way: Slow effects are characterized by an increase for both intensity and delay contralateral to the tapping hand; fast effects are characterized by an increase in activity contralateral to the tapping hand for the delay parameter only (the polarity—positive or negative—of the fast effects cannot be determined, since these effects are analyzed using frequency-domain techniques).

The data reported in Figure 6 suggest that the predicted effects of a layer with increased or reduced scattering or increased absorption vary greatly with the depth of the layer. For the *intensity* parameter, the effects are large for very superficial layers, but they decrease rapidly as depth increases. The simulated results can be fitted quite well ($r > 0.99$) by functions in which the logarithm of the effect of changes in a layer decreases with the square of the distance of the layer from the surface. Layers with increased absorption or scattering determine a reduction in the amount of light reaching the detector with respect to a baseline condition (as shown by the fact that the corresponding fitted curves never go above the baseline level of 1). This suggests that the slow intensity effect observed during tapping cannot be due to an *increase* in absorption or scattering in a particular layer of the head (such as the cortex—scenarios *a*, *c*, and *e*). However, the other two scenarios (*d*: reduced scattering in a particular layer; and *b*: movement of an absorbing substance from more superficial to deeper layers) are both compatible with the observed slow intensity effects. In fact, the Monte Carlo simulations show that intensity is above the baseline level when there is a reduction in scattering in a particular layer. In addition, since a deep absorbing layer lets more light travel between the source and the detector than a superficial absorbing layer, movement of an absorbing substance from a more superficial to a deeper level will result in an increase in intensity.

For the *delay* parameter, the picture is more complex. The delay effects can be better understood by considering that the time-of-travel of individual photons varies and that, in general, photons that travel deeper through the medium take longer to reach the detector than photons that travel more superficially. Further, the effect of changes in the absorbing or scattering properties of layers will be to skew the distribution of the individual photons' travel times either to the left or to the right, depending on the depth of the layer. The fitted curves

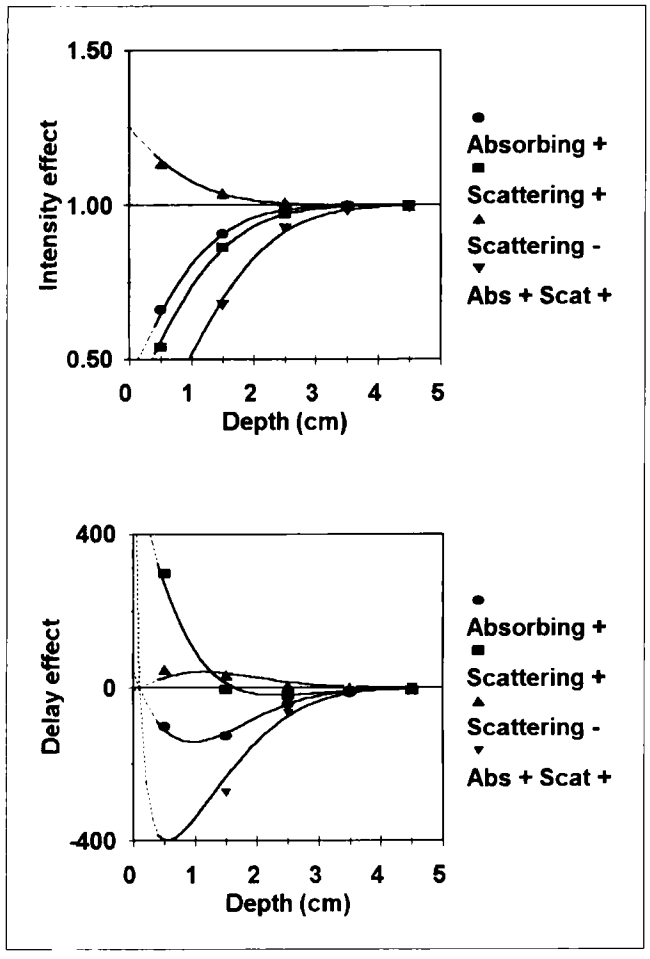

Figure 6. Results of the Monte Carlo simulations (top: intensity; bottom: delay). Data are expressed as deviations from the baseline model (proportional change for intensity, change in picoseconds for delay) for layers at different depths. Circles refer to data obtained by simulating layers with increased absorption (Absorbing +), squares to data obtained by simulating layers with increased scattering (Scattering +), upward triangles to data obtained by simulating layers with reduced scattering (Scattering −), and downward triangles to data obtained by simulating layers with increases for both absorption and scattering (Abs + Scat +). Interpolated lines for intensity imply that the logarithms of the effects of changes in scattering or absorption are inversely related to the square of the distance of the layer from the surface. Interpolated lines for delay imply that changes in scattering or absorption can be modeled by shifts in the distribution of individual photons' travel time. Dashed lines refer to extrapolated segments of the curves.

reported in Figure 6 (delay graph) are obtained in this fashion. Photons that traverse a layer with increased absorption (*circles*) are selectively eliminated (i.e., absorbed), thus shifting the mean of the distribution away from that layer. For this reason, the effect of a deep absorbing layer is to eliminate selectively photons with long travel times, and therefore actually to reduce the average photons' delay. However, given that very few photons travel very deeply, this effect reaches a maximum at a particular depth (in the simulations, this depth is 1–2 cm). A layer with increased absorption located deeper than this level will produce smaller and smaller effects on the delay parameter.

Layers with increased scattering properties also produce similar effects on the distribution of individual photons' travel times: Increases in very superficial layers will delay the photons, by causing an obstacle to their movement. However, an increase in scattering in a deep layer will actually amplify the probability that photons traveling through this layer will be absorbed. This will result in a selective reduction in the number of photons with long travel times, and in shorter average delays. The effects of a layer with reduced scattering are opposite to those of an increased-scattering layer. A reduced-scattering layer will allow photons to travel more deeply and therefore prolong the average delay. However, this effect is limited by an increase in the probability of absorption when photons travel deeply.

The results of the simulations of changes in the delay parameter add boundary conditions for the two scenarios (*b:* movement of absorbing substance to a deeper layer, and *d:* reduced scattering in a layer) that were compatible with the observed changes in intensity. For both of these scenarios, the observed slow delay effect (increase in delay during tapping) is valid only for layers deeper than a minimum value. In fact, scenario *b* predicts a positive slope of the function related to a layer with increased absorption (*circles*), which is true only for the part of the curve to the right of the minimum (in the simulations, for depth greater than 1–2 cm). Scenario *d,* on the other hand, predicts a positive delay for the function related to a layer with reduced scattering (*triangles*), which is true for all but very superficial depths.

The results of the simulations for layers with increases in *both* scattering and absorption show that the effects of these combined increases on both intensity and delay are greater than those produced by the isolated increases in either scattering or absorption. In fact, the results suggest that increases in scattering potentiate the effects of increases in absorption. This is consistent with the idea that increases in scattering act, at least in part, by increasing the probability that photons will be absorbed, and that the combined effects of increases in scattering and absorption on photon migration parameters are, to some extent, multiplicative. This relationship may be used to generate initial predictions about other possible combinations of changes in scattering and absoprtion.

Overall, the results of the simulations for the intensity and delay parameters are consistent with both a reduction in scattering or with movement of an absorbing substance into a deeper layer. For the latter, however, this is true only for layers deeper than 1–2 cm. Note that the delay parameter seems to be more sensitive to changes in deep layers than the intensity parameter. This may provide a possible explanation for the results of the

frequency-domain analysis, showing that fast effects are characterized by changes in delay but not in intensity. In fact, this may happen if the phenomena responsible for the fast effects occur at a relatively deep layer.

DISCUSSION

Our data provide support for the claim that photon migration parameters are sensitive to functional changes in brain activity during a tapping task. Systematic differences emerged between the recordings from locations contralateral and ipsilateral to the tapping limb. Both slow effects (measured across time periods extending over several seconds) and fast effects (reflecting the tapping frequency) were observed. In both cases, lateralization was most evident for hand movements. This is consistent with the functional anatomy of the motor cortex: Since hand areas are located more laterally than foot areas, it was expected that photon migration parameters during hand movements would show more signs of lateralization of function.

A somewhat different pattern emerged for the fast and slow effects. For both, changes were evident for the delay parameter. However, the intensity parameter was involved only in the slow effects. Monte Carlo simulations suggest that these different patterns of results may reflect different underlying mechanisms. Slow effects are consistent with movement of scattering substances to deeper layers, or with reduced scattering. In either case, the simulations suggest that the effect is not very superficial. The fast effects appear also to be consistent with changes in deep layers, although the data are not sufficient to determine the nature of the effects. However, the absence of intensity effects suggests that the fast effects may occur in deeper layers than the slow effects.

The data are insufficient to determine in a conclusive manner the physiological mechanisms underlying the changes in the optical parameters. Possible mechanisms for changes in scattering include variations in the reflectivity or shape of the membranes of the neurons or of other brain cells, or in the accumulation of chemicals that influence the refractive index of brain tissue. Some of these effects may occur very quickly, and thus shadow the tapping frequency. Given the wavelength of the diodes (715 nm), likely candidates for changes in absorption include variations in the concentration of oxy- and/or deoxyhemoglobin. These, in turn, may reflect movement of blood between more superficial and deeper layers, resulting in increased blood flow through the cortex. Increased cortical blood flow is commonly studied with other techniques, such as PET, SPECT, fMRI, and optical observations on exposed cortex (e.g., Belliveau et al., 1991; Grinvald et al., 1986; Raichle, 1994). Indeed, the time course of the slow effects observed is in agreement with that reported with fMRI, which reveals activity in motor areas beginning a few seconds before tapping (presumably reflecting preparatory sets) and lasting for the whole period in which movements occur (Frahm et al., 1995). The time course of the slow effects is also comparable with the "intrinsic" optical signal obtained from the exposed occipital cortex during photic stimulation (Grinvald et al., 1986). This signal is usually attributed to local changes in blood flow (Frostig, 1994).

Noninvasive measures of slow functional changes in brain optical parameters have been reported previously. For example, Kato, Kamei, Takashima, and Ozaki (1993) measured changes of photon migration parameters from occipital regions during photic stimulation. They observed an increased light absorption that started a few seconds after the beginning of the stimulation period, and peaked at the end of this period. However, their recording technique did not allow the detection of faster changes. Furthermore, the stimulation procedure probably also produced changes in heart rate or respiratory patterns (see Coles, Porges, & Donchin, 1986). These, in turn, could have produced changes in the amount of blood in various areas inside and outside the brain, thus affecting the amount of light reaching the detector. Note that such changes may also have occurred during our experiment. An appropriate control for nonspecific effects is required before changes in photon migration parameters can be ascribed to changes in brain metabolism. In the study by Kato et al. (1993) a frontal probe was used. In the study reported in the present paper we chose to counterbalance the side of the limb with which the subject was requested to tap. Furthermore, measures were taken from locations contralateral and ipsilateral to the limb used for tapping. We reasoned that nonspecific effects (such as changes in autonomic activity) would influence the measurements in a similar fashion regardless of whether the movements were performed with the ipsilateral or contralateral limb (e.g., the relationship between the two sides would remain constant). On the other hand, since the motor system is crossed, changes due to cortical involvement would produce asymmetries that would change direction systematically depending on the movement side (e.g., the effects would always be greater at the recording sites contralateral to the moving limb, irrespective of whether the movement was made with the left or right limb). Note that in this fashion each location is used as its own control.

No significant difference was observed between contralateral and ipsilateral foot tapping. Note, however, that foot tapping appeared to exert a bilateral effect on the intensity parameter (only a contralateral effect was observed for hand tapping). This suggests that the absence of lateralization effects for foot tapping might have occurred either because the projection areas for left and right foot movements are too close to be separated by our recording procedures, or because foot tapping involves both hemispheres to a similar degree.

Taken together, the results support the claim that measures of optical parameters provide evidence of

rapid physiological changes in the brain during motor tasks. The system dynamics allow us to track functionally significant brain phenomena with a frequency of at least 0.8 Hz. This indicates that photon migration measures are potentially quite fast with respect to blood flow measures based on radioactive tracers (such as PET and SPECT), and at least as fast as fMRI (see Belliveau et al., 1991; Churchland & Sejnowski, 1988). However, since the measures were not time-locked to the subjects' movements, it is not possible to determine the latency of the optical changes with respect to brain activity. Deriving time-locked waveforms depicting the time course of changes in optical parameters with respect to external (or internal) events appears to be an important direction for future research.

Both fast and slow effects were more evident when the recordings were taken from the right hemisphere (although the recording side by tapping side interaction never reached significance). Greater lateralization for right hemisphere recordings during hand movements was also obtained by Kim et al. (1993) using fMRI. Remy et al. (1994), using PET data, also observed greater contralateral activity for non-dominant-hand movements than for dominant-hand movements, although this difference did not reach significance. This provides additional support for the claim that noninvasive optical recordings provide a simple tool for studying brain function, and that they can discriminate between activity in the left and right hemisphere. Coupled with low cost and noninvasivity, these properties make the estimation of photon-migration parameters a promising new tool for the study of the dynamics of brain metabolic activity during cognitive and behavioral tasks. They may be particularly useful for the integration of electrophysiological and metabolic data.

METHODS

Task

The measures were taken on four right-handed healthy male volunteers (age range 25-55), over two sessions. Each session included four types of trials, repeated three to five times: tapping with the left foot, tapping with the left hand, tapping with the right foot, and tapping with the right hand. Each trial comprised three periods: 10 sec of rest, 20 sec of tapping, and 10 sec of rest. A metronome was turned on during the tapping period, and subjects were instructed to follow the metronome's beat to maintain a tapping frequency of 0.8 Hz. A 50-sec rest interval was provided between trials.

Optical Recordings

Near-infrared light was produced by one of two light emitting diodes (LEDs) that was secured on the subject's head by means of a helmet. The light's peak wavelength (715 nm) was chosen to be equally sensitive to oxy- and deoxyhemoglobin. The diodes abutted the surface of the scalp approximately 3 cm to the left and right of the vertex (Cz location of the International 10-20 System). These locations are close to the primary motor areas responsible for hand and foot movements. In the first session, the left diode was used as a source, while the right one was used in the second session. The detector, connected to a photomultiplier, was a fiber optic (diameter 0.5 cm) placed over the vertex. The average power of the diodes was 300 μW. The intensity of the light emitted by the diodes was modulated using a radiofrequency wave synthesizer at 60 MHz for the first three subjects (who were run at the University of Illinois), and 112 MHz for the fourth subject (who was run at Columbia University).[4] The voltage applied to the photomultiplier used as detector (which determined its gain) was also modulated using a frequency that differed from that used for the diodes by 1000 Hz. This pair of beating frequencies allowed the amplitude modulations of the light wave to be reflected in the 1000 Hz range, well within the capabilities of the A-D converter. The parameters related to the statistical distribution of the photon time-of-flight (average delay and coherence of the amplitude modulated signal) were then computed digitally (Gratton et al., 1990). Measures of *DC intensity* (average intensity for each cycle) and *phase* difference between input and output signal (assessing the average delay of the amplitude modulated signal) were obtained every 80 msec (sampling frequency = 12.5 Hz). The phase delay data were then transformed in picoseconds before further analyses were performed. The heart beat, or pulse, artifact was attenuated using a procedure described in Gratton and Corballis (1995). Three trials from subject 4 were excluded from the analysis because of large variability in the delay parameter, presumably due to artifacts.

Monte Carlo Simulations

The model used for the Monte Carlo simulations is based on representing photon movements by a three-dimensional random walk in a discrete cubic lattice. The size of the elementary cell is comparable with the transport mean free path. In a typical run, 3×10^7 particle trajectories are calculated. The time of arrival of photons at the detector is stored using a time histogram of 1024 time channels. The Fast Fourier Transform algorithm is used to calculate the frequency domain parameters. This model is similar to that used by Bonner, Nossal, Havlin, and Weiss (1987). Boundary conditions, such as those caused by a scattering or absorbing layer, are easily introduced into the model by specifying, for each cell of the lattice, the local value of the scattering and absorption coefficients (i.e., layers are defined by abrupt changes in the values of scattering or absorption parameters). The head is approximated by a semiinfinite medium, which can be specified in the model by allowing

photons to move only in one half-space. This model has been shown to provide an accurate description of the photon trajectories and of the photon density at each point in the lattice (Bonner et al., 1987). All of the simulations are based on a uniform scattering medium with μ_a = 0.05 cm^{-1} (coefficient of absorption) and μ_s = 5.0 cm^{-1} (coefficient of scattering). Both of these values were based on the average of preliminary measures taken on the forehead of 15 subjects at rest. In each simulation (apart from the baseline model) a layer 1 cm thick, parallel to the medium surface, is inserted into the scattering medium. This layer differed by a factor of 2 from the rest of the medium in terms of either the scattering (scattering layer) or the absorption (absorbing layer) coefficient. The modulation frequency was set at 118 MHz.

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Notes

1. We thank one of the anonymous reviewers for suggesting this analysis.
2. Note that changes in absorption can be due either to fluctuations in blood flow or to variations in the absorption spectrum of the blood, such as those due to changes in the blood oxygenation level.
3. Preliminary observations suggest that changes in intensity and phase obtained with these values of absorption and scattering are representative of changes obtained in a wide range of scattering and absorption conditions.
4. Since the pattern of results obtained was similar for all subjects, they were combined for data analysis.

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