Long-Term Changes in Optical Properties (μ_a, μ_s', μ_{eff} and DPF) of Human Head Tissue During Functional Neuroimaging Experiments

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Abstract

Frequency-domain near-infrared spectroscopy (FD-NIRS) enables to measure absolute optical properties (i.e. the absorption coefficient, μ_a, and the reduced scattering coefficient, μ_s') of the brain tissue. The aim of this study was to investigate how the optical properties changed during the course of a functional NIRS experiment. The analyzed dataset comprised of FD-NIRS measurements of 14 healthy subjects (9 males, 5 females, aged: 33.4 ± 10.5 years, range: 24–57 years old). Each measurement lasted 33 min, i.e. 8 min baseline in darkness, 10 min intermittent light stimulation, and 15 min recovery in darkness. Optical tissue properties were obtained bilaterally over the prefrontal cortex (PFC) and visual cortex (VC) with FD-NIRS (Imagent, ISS Inc., USA). Changes in μ_a and μ_s' were directly measured and two parameters were calculated, i.e. the differential pathlength factor (DPF) and the effective attenuation coefficient (μ_{eff}). Differences in the behavior of the optical changes were observed when comparing group-averaged data versus single datasets: no clear overall trend was presented in the group data, whereas a clear long-term trend was visible in almost all of the single measurements. Interestingly, the changes in μ_s' statistically significantly correlated with μ_a, positively in the PFC and negatively in the VC. Our analysis demonstrates that all optical brain tissue properties (μ_a, μ_s', μ_{eff} and DPF) change during these functional neuroimaging experiments. The change in μ_s' is not random but follows a trend, which depends on the single experiment and measurement location. The change in the scattering properties of the brain tissue during a functional experiment is not negligible. The assumption $\mu_s' \approx$ const during an experiment is valid for group-averaged data but not for data from single experiments.

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1   Introduction

Functional near-infrared spectroscopy (fNIRS) is a non-invasive neuroimaging technique measuring cerebral blood oxygenation and perfusion [1]. An absolute quantitation of the concentration of oxyhemoglobin ([O_2Hb]) and deoxyhemoglobin ([HHb]) is possible applying the frequency-domain near-infrared spectroscopy (FD-NIRS) technique. The optical properties of tissue, namely the absorption coefficient (μ_a) and reduced scattering coefficient (μ_s'), provide information on the state and composition of the investigated tissue. Two additional parameters characterizing the optical properties of the tissue are the effective attenuation coefficient (μ_{eff}) and differential pathlength factor (DPF). While μ_{eff} is sufficient for determining light attenuation in the diffusion regime and is proportional to the geometric mean of μ_a and μ_s', DPF is defined as the scaling factor that relates source-detector separations (SDS) to the average path length light travels between the source and detector. To date, most fNIRS studies in humans using continuous-wave near-infrared spectroscopy (CW-NIRS) devices rely on an assumed constant DPF and μ_s' during the measurement, an assumption not necessarily true in reality. Any fNIRS quantification of tissue oxygen saturation and hemodynamics that assumes a constant DPF and μ_s' will be erroneous when the DPF and μ_s' change over time.

The aim of this study was to monitor changes in absolute optical properties in human head tissue during a neuroimaging experiment.

2   Material and Methods

The dataset for the present analysis comprised FD-NIRS measurements of 14 healthy subjects (9 males, 5 females, aged 33.4 ± 10.5 years, range 24–57 years old) obtained during a neuroimaging study recently conducted [2]. The study investigated stimulus-evoked changes in cerebral hemodynamics and oxygenation elicited by wide-field visual color stimulation with three different colors. Each measurement lasted 33 min (i.e. 8 min baseline in darkness, 10 min intermittent light stimulation, and 15 min recovery in darkness).

A multi-channel FD-NIRS system with multi-distance approach (Imagent, ISS Inc., Champaign, IL, USA) was employed to measure absolute μ_a and μ_s' of tissue bilaterally at the prefrontal cortex (PFC; Fp1 and Fp2) and the visual cortex (VC; RVC and LVC).

For the present analysis, data from the whole data set were selected that did not contain movement artifacts and had a high signal-to-noise ratio (indicated by the absolute light intensity values recorded at the detectors) of the μ_a and μ_s' signals for both measurements at the PFC and VC. A total of 31 single experiments were analyzed. For the analysis, the $\Delta\mu_a$ and $\Delta\mu_s'$ signals were downsampled to 1.25 Hz to reduce the high-frequency noise. From the μ_a and μ_s' signals, two additional signals were calculated afterward to quantify the tissue optical properties with two additional parameters: DPF and μ_{eff}, given as

$$\text{DPF} = 1/2\sqrt{3\mu_s'/\mu_a} \text{ and } \mu_{eff} = \sqrt{3\mu_a\left(\mu_a + \mu_s'\right)}.$$

All the subsequent processing steps were performed for μ_a, μ_s', μ_{eff} and DPF. Signals from the left and right PFC as well as VC were averaged to obtain signals for the whole PFC and VC, respectively. To analyze the long-term (i.e. minute) trend of the signals, the signals were first normalized (by subtracting the median value of the first 3 min from each time point), and then a group-average (median ± confidence intervals) of all experiments was calculated. The normalized signals are indicated by a 'Δ'. Changes in the signals were quantified (stimulus interval vs. baseline, recovery vs. stimulus interval, and recovery vs. baseline) by calculating the median values during the specific time intervals and by performing a statistical analysis (Wilcoxon signed-rank test, corrected for multiple comparisons). Individual changes in the signals were also analyzed.

Finally, the correlations of the long-term changes in the optical signals were determined (Spearman correlation) for the following signal combinations (for both PFC and VC and for both wavelengths): $\Delta\mu_s'$ vs. $\Delta\mu_a$, $\Delta\mu_s'$ vs. $\Delta\mu_{eff}$, $\Delta\mu_s'$ vs. ΔDPF, $\Delta\mu_a$ vs. ΔDPF, $\Delta\mu_a$ vs. $\Delta\mu_{eff}$, and $\Delta\mu_{eff}$ vs. ΔDPF.

3   Results

The group-averaged long-term changes of the optical signals, μ_a, μ_s', μ_{eff} and DPF, exhibited mainly three features (Fig. 1): (i) no clear overall trend was present (the analysis of the comparisons of signal intervals revealed no statistically significant trend; Fig. 3a–d), (ii) stimulus-evoked changes in μ_s' and μ_{eff} were visible at the onset of the visual stimulation block (increase in $\mu_s' \approx 0.02\,\mathrm{cm}^{-1}$ and increase in $\mu_{eff} \approx 0.01\,\mathrm{cm}^{-1}$, at 760 nm), and (iii) evoked changes were only visible in the signals from the PFC and not from the VC.

When looking at the changes in μ_a, μ_s', μ_{eff} and DPF in the single datasets the following features were evident (Fig. 2): (i) a clear long-term trend was visible in almost all of the datasets; (ii) non-random i.e., physiological changes were present in the data of the PFC and the VC; and (iii) the changes varied in a non-systematic manner between subjects.

Concerning the correlations of the long-term changes of optical parameters an interesting phenomenon was observed: (Fig. 3e–f): $\Delta\mu_s'$ and $\Delta\mu_a$ correlated statistically significantly positively in the PFC and negatively at the VC. The difference was statistically significant by itself for both wavelengths. The other correlations were positive ($\Delta\mu_s'$ vs. $\Delta\mu_{eff}$, $\Delta\mu_s'$ vs. ΔDPF, $\Delta\mu_a$ vs. $\Delta\mu_{eff}$) and negative ($\Delta\mu_a$ vs. ΔDPF, $\Delta\mu_{eff}$ vs. ΔDPF).

4   Discussion and Conclusions

The assumption that μ_s' as well as the DPF do not change systematically during a neuroimaging experiment with fNIRS is not valid. There is a large variability of μ_s' discernable when analyzing individual datasets from single experiments. The variability is greatly reduced by group-averaging of the data; however, stimulus-evoked changes in μ_s' and μ_{eff} were also clearly detected in this case at the PFC. Changes in μ_s' are not surprising during a period of increased tissue hemoglobin content (intermittent light stimulation) since the changes in the shape of the blood vessels (e.g. diameter) and the increased number of red blood cells lead to an increase in the scattering properties of the tissue [3]. But changes in scattering were not necessarily accompanied by significant changes in the absorption (Fig. 1). In addition, changes in glucose in the tissue may lead to changes in μ_s' [4]. Differences in μ_s' variability between PFC and VC (Fig. 1) may be attributed to differences in the brain activation and other physiological processes between these regions, structural anatomical differences (vessel density and skull thickness) and the smaller light intensity at the detector in the VC compared to the PFC due to hair, which leads to a lower signal-to-noise ratio and hence higher variability in the VC. The predominant error of the ISS Imagent is the shot noise and the error of measurement thus depends on the number of photons measured. The lower penetration depth of NIRS at the VC due to a higher μ_s' is expected to even reduce the variability in the VC. Fast transient increases in μ_s' at the onset of visual stimulation have been reported by various research groups [3]. The changes in μ_{eff} observed can be attributed to changes in μ_s' and μ_a. Concerning the variation of DPF, it has been reported that the DPF at 761 nm depends on oxygenation and is positively related to the arterial oxygen saturation (SaO_2) and sagittal sinus venous oxygen saturation (SvO_2) [5]. The finding in our study that μ_s' changes were positively correlated with μ_a changes at the PFC and negatively at the VC is unexpected and requires further investigation.

Concerning the question whether the magnitude of the changes in μ_s' is relevant for the correct determination of [O_2Hb] and [HHb], in CW-fNIRS studies it can be concluded that a stimulus-evoked changing of 0.02 in μ_s' (as observed in our study, Fig. 1a) corresponds to a 0.12 μM change in [O_2Hb] assuming an absolute O_2Hb concentration of 60 μM. Since a normal stimulus-evoked change of [O_2Hb] during a neuroimaging experiment is in the order of 0.1 μM, such a change in μ_s' is relevant. The long-term changes of μ_s', having an even
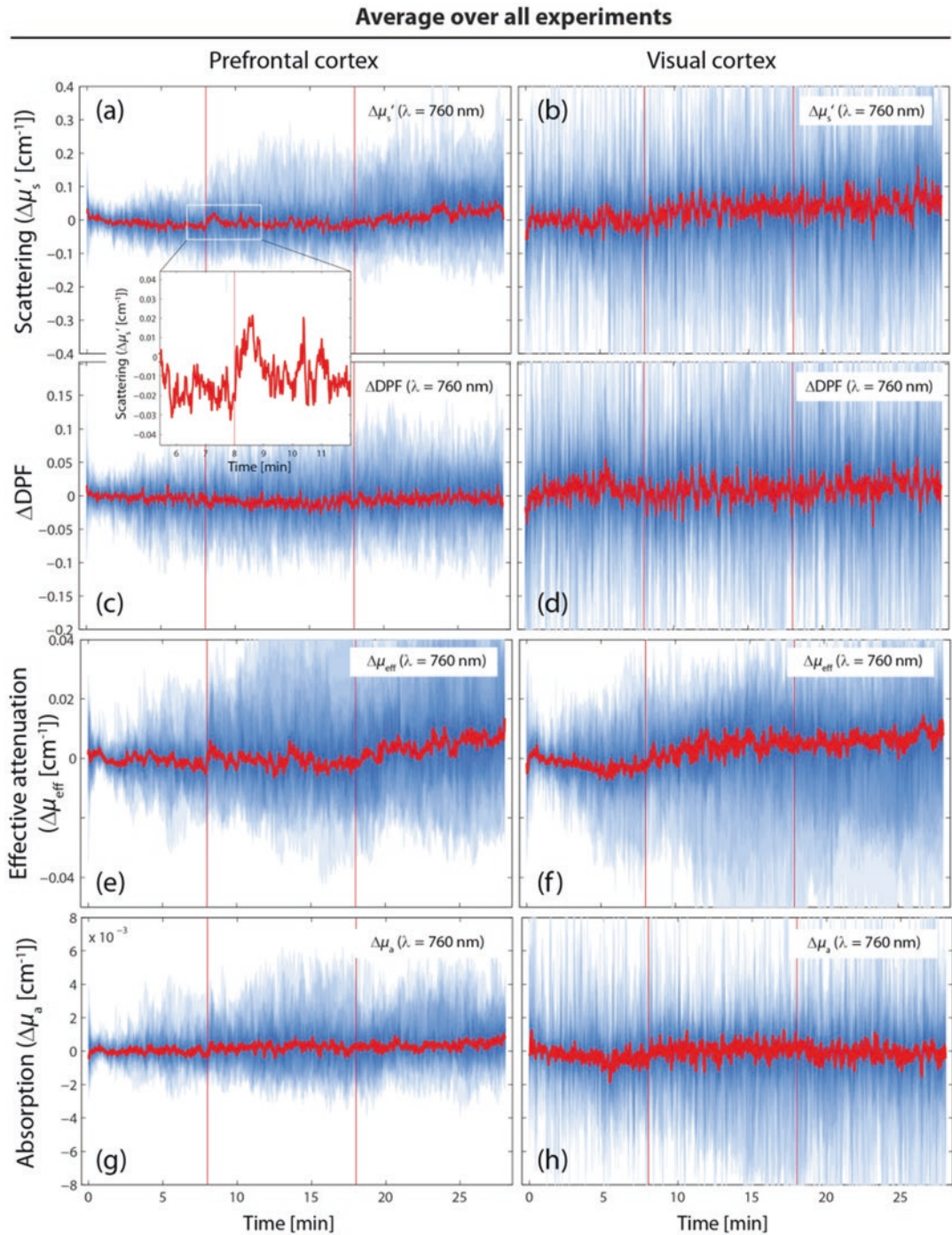
Average over all experiments

Fig. 1 Time-series of the group-averaged relative changes in the optical properties ($\Delta\mu_s'$, ΔDPF, $\Delta\mu_{eff}$, $\Delta\mu_a$) of the prefrontal cortex (PFC) and the visual cortex (VC) at 760 nm. Data are shown as median values and the 95% confidence interval (blue area). One segment of (**a**) is zoomed in, indicating a stimulus-evoked change in $\Delta\mu_s'$
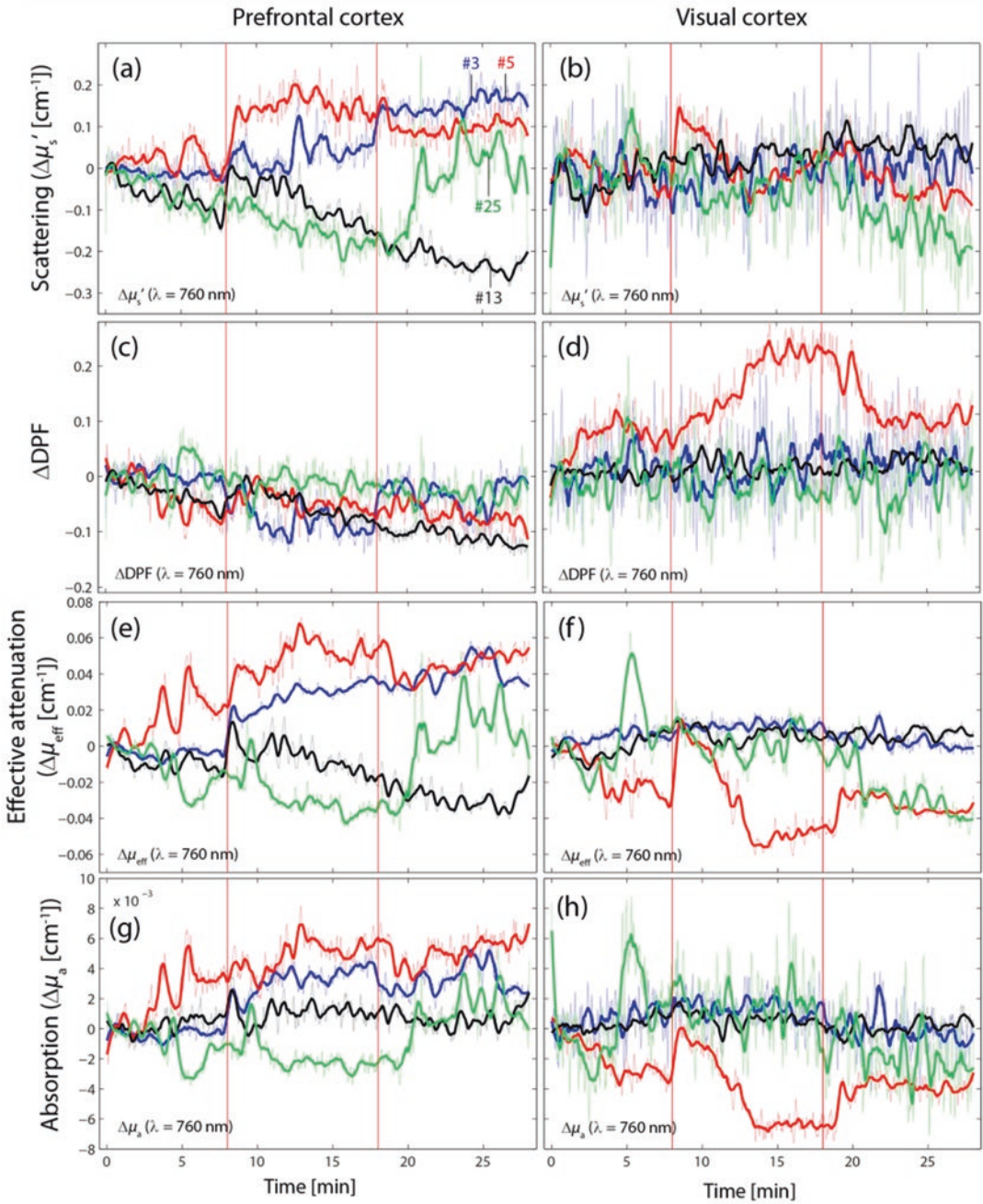
Fig. 2 Time series of the *single dataset* relative changes from four trials (with a different subject each; trials: #3, #5, #13, and #25) in the optical properties ($\Delta\mu_s'$, ΔDPF, $\Delta\mu_{eff}$, $\Delta\mu_a$) of the prefrontal cortex (PFC) and the visual cortex (VC) at 760 nm
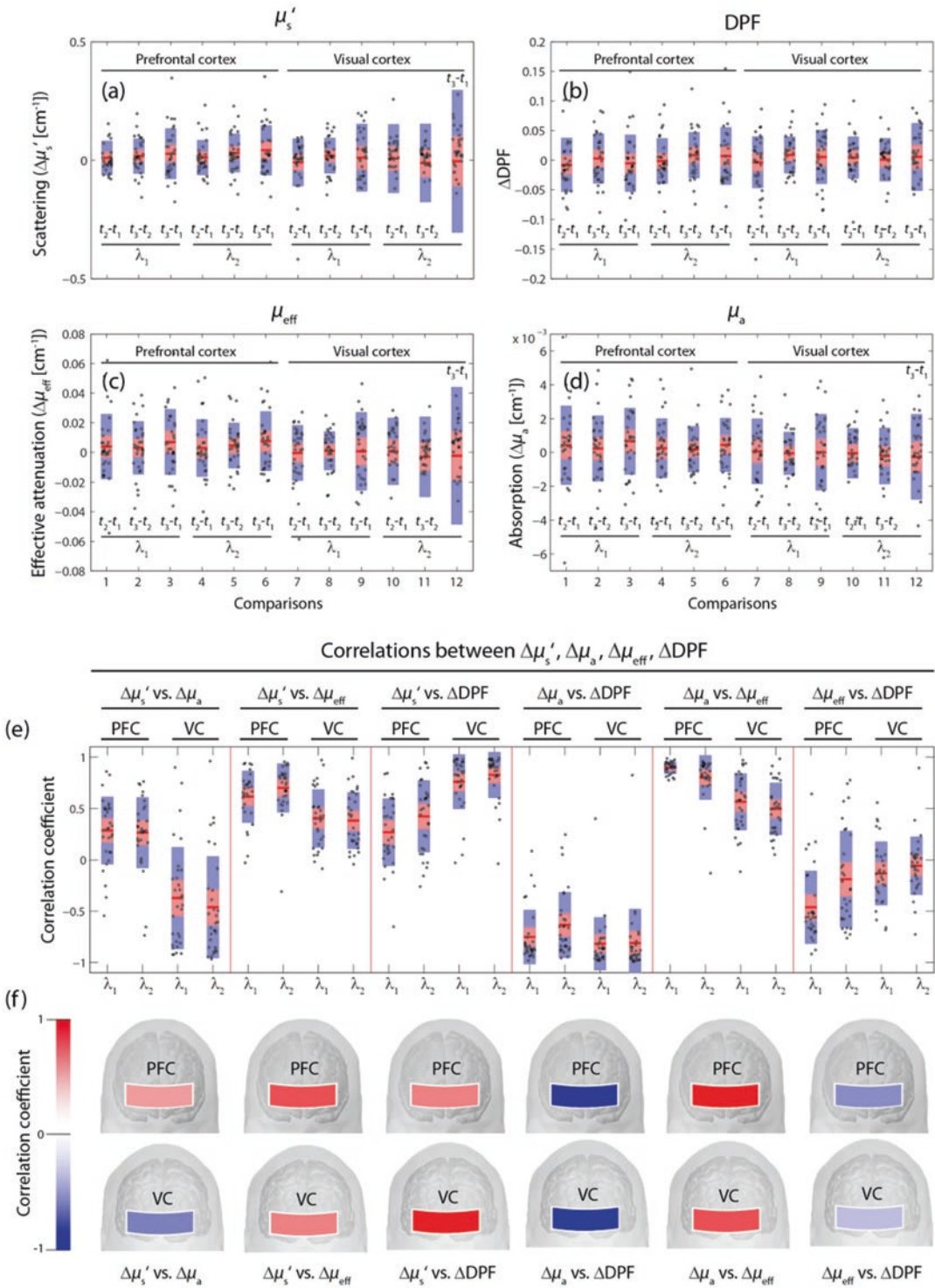
Fig. 3 Overview of the changes in the optical signals ($\Delta\mu_s'$, ΔDPF, $\Delta\mu_{eff}$, $\Delta\mu_a$) of the prefrontal cortex (PFC) and the visual cortex (VC) at two wavelengths ($\lambda_1 = 760$ nm, $\lambda_2 = 830$ nm) quantified by calculation of the median values during the specific time intervals (t_1: baseline; t_2: stimulus interval; t_3: recovery) (**a–d**). Correlations of the long-term changes in the optical parameters for both measurement locations (PFC and VC) and at two wavelengths (**e–f**)

higher magnitude (especially when looking on individual measurements), are relevant for CW-fNIRS studies that investigate the long-term changes in [O$_2$Hb] and [HHb] (i.e. resting-state fNIRS studies or NIRS-oximetry applications for patient monitoring). In conclusion, we found that changes in the scattering properties of the brain tissue during a functional experiment are not negligible, especially in single datasets; the assumption $\mu'_s \approx$ const during an experiment is valid for group-average data but not for data from single experiments. Moreover, in this particular type of functional NIRS experiments, we recommend using FD-NIRS or time-domain NIRS systems instead of CW-NIRS, since these techniques are able to measure the time-dependence of μ'_s directly. Finally, the authors believe that further research is warranted to understand the exact effects of changes in optical properties on the changes in [O$_2$Hb] and [HHb].

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