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Reconstructing functional near-infrared spectroscopy (fNIRS) signals impaired by extra-cranial confounds: An easy-to-use filter method

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ABSTRACT

Functional near-infrared spectroscopy (fNIRS) is an optical neuroimaging method that detects temporal concentration changes of oxygenated and deoxygenated hemoglobin within the cortex, so that neural activation can be inferred. However, even though fNIRS is a very practical and well-tolerated method with several advantages particularly in methodically challenging measurement situations (e.g., during tasks involving movement or open speech), it has been shown to be confounded by systemic compounds of non-cerebral, extra-cranial origin (e.g. changes in blood pressure, heart rate). Especially event-related signal patterns induced by dilation or constriction of superficial forehead and temple veins impair the detection of frontal brain activation elicited by cognitive tasks. To further investigate this phenomenon, we conducted a simultaneous fNIRS–fMRI study applying a working memory paradigm (n-back). Extra-cranial signals were obtained by extracting the BOLD signal from fMRI voxels within the skin. To develop a filter method that corrects for extra-cranial skin blood flow, particularly intended for fNIRS data sets recorded by widely used continuous wave systems with fixed optode distances, we identified channels over the forehead with probable major extra-cranial signal contributions. The averaged signal from these channels was then subtracted from all fNIRS channels of the probe set. Additionally, the data were corrected for motion and non-evoked systemic artifacts. Applying these filters, we can show that measuring brain activation in frontal brain areas with fNIRS was substantially improved. The resulting signal resembled the fMRI parameters more closely than before the correction. Future fNIRS studies measuring functional brain activation in the forehead region need to consider the use of different filter options to correct for interfering extra-cranial signals.

Introduction

Using functional near-infrared spectroscopy (fNIRS) neural activation is indirectly measured by determining the NIR-light attenuation between an emitter–detector pair placed on the subject's head surface, mostly in a distance of 3 cm to achieve adequate depth of NIR-light penetration (Ferrari and Quaresima, 2012). Biological tissue is a highly scattering optical medium with relatively low absorption characteristics, enabling a measurable amount of light to reach the detector. Since the main light absorbers in this setup are the two types of hemoglobin, changes in measured light intensity can be related to hemodynamic changes, which are coupled to neural activation (neurovascular coupling, Logothetis and Wandell, 2004).

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Cerebral and extra-cranial signal contributions

The measuring principle of continuous-wave fNIRS can be described by a modified Beer–Lambert law introduced by Delpy et al. (1988) (for a more detailed description see Obrig and Villringer (2003) or Scholkmann et al. (2014)). To distinguish between the two types of hemoglobin usually two different wavelengths are used. The time-dependent measured light attenuation

$$A_{total}(t) = -\ln\frac{I_D}{I_E} = \langle L\rangle \mu_a(t) + A_{scattering} \quad (1)$$

for a certain wavelength consists of an absorption (left hand side of the sum) and a scattering term (right hand side of the sum). Whereas I_D is the detected light intensity and I_E is the emitted light intensity, $<L>$ is the mean optical path length and $\mu_a(t)[\mathrm{mm}^{-1}]$ is the absorption rate. It has shown to be a reasonable approximation to assume the optical path lengths as time-independent (Sassaroli and Fantini, 2004). By

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considering only temporal changes of $A_{total}(t)$ the time-independent scattering term can be eliminated. As we assume the concentrations of the main NIR-light absorbers in biological tissue (i.e. oxy-Hb and deoxy-Hb) to change considerably only within the skin and gray brain matter, the differentials of light absorption coefficients are negligible for all remaining tissue types (i.e. skull, cerebral spinal fluid, white brain matter). Hence, the temporal differential of the total light attenuation in this setup, i.e. the measured fNIRS signal, can be written as

$$dA_{total}(t) = \langle L_{skin} \rangle d\mu_{a,skin}(t) + \left\langle L_{gray} \right\rangle d\mu_{a,gray}(t), \quad (2)$$

Where $<L_{skin}>$ and $<L_{gray}>$ are the mean optical path lengths through the skin and gray brain matter, respectively. The $d\mu_{a,skin}(t)$ and $d\mu_{a,gray}(t)$ are temporal differentials of the respective tissue absorption coefficients. Since oxy-Hb and deoxy-Hb are the main absorbers of the emitted wavelengths, these absorption coefficients indicate concentration changes of oxy-Hb and deoxy-Hb in the skin and gray brain matter and are thus indirectly related to hemodynamics – i.e. changes in blood volume, oxygenation and flux – in the respective tissue. Henceforth, we refer to hemodynamics in gray brain matter and skin as cerebral blood flow (CBF) and skin blood flow (SBF), respectively. Each of these hemodynamic terms is weighted by the respective optical path length, i.e. the averaged distance the light travels between emitter and detector. Based on previous simulations (Haeussinger et al., 2011) the ratio $<L_{skin}>:<L_{gray}>$ roughly amounts to 20:1, indicating that fNIRS is about twenty times more sensitive to SBF than to CBF.

Effect of extra-cranial signals

The disturbing influence of SBF on the measurement of brain activation by fNIRS during mental tasks has already been addressed. By combining fNIRS with Laser Doppler flowmetry Harris et al. (1994a) could show that fNIRS in the temporal region is strongly influenced by the hemodynamics of the external carotid artery. Conducting an fNIRS study with a verbal fluency task, Takahashi et al. (2011) simultaneously assessed SBF by adding short-distance optodes (0.5 cm distance) and showed that the largest part of the measured fNIRS amplitude (3.0 cm distance) on the forehead was evoked by SBF changes. The event-related signal change of CBF and SBF showed the same shape resulting in an over-estimation of brain activation. In another study, Kirilina et al. (2012) compared brain activation during a working memory task (n-back) measured successively with fMRI and fNIRS. Inconsistencies between activation patterns (fNIRS showed a systematic deactivation instead of an expected activation) were explained by the authors by an event-related signal decline in oxy-Hb mostly apparent in the fronto-polar region. Interpreting the BOLD signal in skin voxels as extra-cranial signal, the origin of this event-related pattern could be located in skin veins in the fronto-polar region. Combining simultaneous fNIRS–fMRI with short optode distance fNIRS and Laser Doppler flowmetry, Sato et al. (2013) showed that fNIRS reflects not only CBF but also SBF. Besides fNIRS and Laser Doppler flowmetry Sorensen et al. (2012) ascertained the cerebral capillary oxygenation by catheters and found an extra-cranial impact on fNIRS in the forehead region when delivering norepinephrine to the subjects. This indicates an influence of the sympathetic nervous system that induces a cutaneous vasoconstriction in the active state.

Time-resolved fNIRS (Liebert et al., 2004) is an optical neuroimaging method measuring the photons' time of flight between source and detector. In practice, the temporal spreading of light pulses is quantified. It is reasonable to assume that photons with shorter flight times mainly traversed more superficial tissues such as skin and skull, whereas those photons with a longer travel duration reached also deeper regions such as brain tissue. Evoking a strong global vascular response by a Valsalva maneuver, Aletti et al. (2012) showed that the signal of the early photons reflects mainly SBF on the forehead as measured by Laser Doppler flowmetry. This shows that fNIRS on the forehead can be disturbed by extra-cranial influences, but it also shows that time-resolved fNIRS is a promising tool for optical neuroimaging, since it can – in contrast to continuous-wave fNIRS – better distinguish between intra- and extra-cranial signals.

Different filter approaches

One attempt to correct for SBF is based on the finding that the amount and ratio of light-absorbing extra- and intra-cranial tissues depend on the emitter–detector distance (Harris et al., 1994b; Fantini et al., 1994; Okada et al., 1997; Fukui et al., 2003; Yamada et al., 2009). For shorter (i.e. <1.0 cm to 1.5 cm) distances nearly no light from gray brain matter reaches the detector, thus, these signals almost exclusively consist of extra-cranial compartments and can consequently be used for SBF correction (Gregg et al., 2010; Saager et al., 2011; Takahashi et al., 2011). An ideal fNIRS measurement setup should therefore include long and short emitter–detector distances per channel. Unfortunately, currently deployed multi-channel fNIRS-systems only provide single and fixed optode distances (usually 3.0 cm) limiting the potential use of this kind of SBF correction.

Furthermore, fNIRS signals can also be influenced by systemic effects such as blood pressure changes (Minati et al., 2011b; Moody et al., 2005; Tachtsidis et al., 2008) or the partial pressure of carbon dioxide in the arterial blood (Scholkmann et al., 2012). To address these effects, another approach to face extra-cranial compounds was proposed by Tachtsidis et al. (2010) and Patel et al. (2011) by combining fNIRS data with simultaneously assessed systemic measures (e.g. like blood pressure, respiration, heart rate and SBF). However, these methods have the disadvantage that additional hardware needs to be installed, thus constraining the inherent advantages of the fNIRS method, i.e. flexibility and efficiency.

Motion artifacts represent another important factor reducing fNIRS data quality, for which different approaches of artifact correction have been proposed, for example, designs including additional simultaneous measurements, such as accelerometer measurement (Virtanen et al., 2011) or short-distance fNIRS measurement (Robertson et al., 2010). Other methods do not rely on additional equipment and are consequently more convenient. For instance, they use principal component analysis (Zhang et al., 2005), wavelet transform (Molavi and Dumont, 2012) or moving standard deviation (Scholkmann et al., 2010). An interesting and especially easy to apply method is the correlation based signal improvement (CBSI) proposed by Cui et al. (2010). Here, a new time series – basically a linear combination of the oxy-Hb and deoxy-Hb time series – is computed. In this way not only motion artifacts are reduced but also non-evoked systemic influences such as heart rate, Mayer waves or very low frequency oscillations (Scholkmann et al., 2014).

Proposal for an extra-cranial filter approach

In this paper, we introduce a rather easy method for multi-channel frontal optode arrangements (including the forehead) which allows the reconstruction of signals that are distorted by SBF. This method is based on the assumption that there are specific probe-set channels over the fronto-polar area which mainly measure SBF – besides CBF – and which are strongly influenced by anatomical barriers, i.e. frontal sinus and increased scalp-cortex distance (Haeussinger et al., 2011). To correct consequently for SBF, the oxy-Hb signal of these channels is averaged and subtracted from the oxy-Hb time series of all channels of the probe set. This procedure is restricted to oxy-Hb signals, as we know from Heinzel et al. (2013) or Kirilina et al. (2012) that the deoxy-Hb time series is hardly affected by SBF. To correct for motion artifacts and non-evoked systemic signals, the skin-corrected oxy-Hb time series are combined with the respective raw deoxy-Hb time series using CBSI (Cui et al., 2010). This combined filter method is especially