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GLM analysis of time resolved NIRS data of motor activation during different motor tasks

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***Abstract*— The hemodynamic response to motor activation was investigated by time-resolved NIRS in healthy subjects and patients with unilateral impairment in motor ability. Healthy subjects performed a simple and a complex finger movement task, patients a handgrip task. A General Linear Model approach (GLM) was applied during NIRS data processing. In general, compared to the integral (continuous wave signal), higher significance of activation was found for the variance signal that selectively represents changes in the deep compartment. A discussion of GLM results with respect to task complexity and difficulty is provided.**

I. Introduction

General Linear Models (GLM) are a statistical tool which has found wide employment in neuroscience, and specifically in the functional Magnetic Resonance Imaging, for the investigation of cortical activation [1]. Consequently, its employment has been extended to the field of near-infrared spectroscopy (NIRS) data processing, for the study of physiological hemodynamics in the brain, and for clinical research [2-3]. In this contribution we present preliminary results of GLM performance for tasks of different complexity and difficulty. Indeed, we considered two different factors affecting the execution of the task: (i) an intrinsic one, consisting in the specific motor request of the task and affecting complexity, and (ii) an extrinsic one, consisting in the partial impairment to execute the motor request, due to a pathological condition, and thus also affecting the difficulty to accomplish the task.

A group of healthy volunteers, performing two versions of a hand motor task, differing in the motor request, and a group of patients with stroke diagnosis were enrolled in the studies.

II. Materials and Methods

A. NIRS instrumentation

Both studies were designed as a combination of simultaneous time-resolved NIRS (trNIRS) and DC-MEG measurements in a setting similar to [4]. The analysis presented here is focused on the trNIRS data, thus only details of the trNIRS measurement are reported. Time-of-flight distributions of photons were recorded with the time-domain NIR imager described in [5]. The wavelengths of the picosecond diode lasers were 687 nm, 803 nm and 826 nm. Time-resolved diffuse reflectance was recorded by time-correlated single photon counting in the four detection channels in parallel (see Fig. 1), with a collection time of 50 ms in a continuous sequence. The count rate was adjusted to values between 2 MHz and 3 MHz, if possible. The detector optodes were arranged in a cross-like shape with source-detector separations of 3 cm. The optode pad was positioned above the left or right motor cortex (C3 or C4 according to the 10-20 system, respectively) of the supine subject.

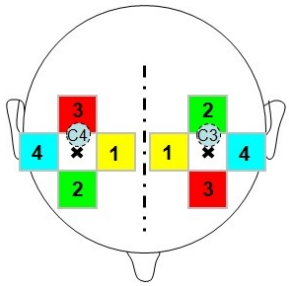

Figure 1. Location of detector optodes (numbers) over the two brain hemispheres. The two probes were fitted so as to locate C3 or C4 standard position midway between source (cross) and posterior detector.

B. fNIRS data processing

From the measured series of time-of-flight distributions of photons, time series of statistical moments of these distributions were extracted, in particular integral and variance. *Variance* (second central moment) has a selective sensitivity to deep absorption changes and provides a suitable representation of cerebral signals [5]. The *integral* corresponds to a continuous wave (cw) NIRS measurement and is sensitive to both deep and superficial changes with a higher sensitivity to the latter. From the time series at the various wavelengths, the time courses of HbO and HbR changes were obtained, separately for integral and variance. Overall amplitude changes were quantified after block averaging, by taking the mean value during the plateau of the response (between 10 s after onset and end of the motor stimulation) and subtracting the mean of the corresponding rest phase.

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A General Linear Model (GLM) approach was applied for data analysis [1]. Data processing was performed by means of NIRS-SPM v.4 software [2]. A hemodynamic response function (HRF) peaking at 6 s was chosen. The wavelet Minimum Description Length (MDL) detrending algorithm (4 coefficients) was applied, aiming at avoiding the removal of task-related oscillations. No correction for serial correlations was performed. A design matrix was used, containing the regressor modeling the activation blocks of the motor task and the default constant regressor for offset removal. A contrast array was designed to investigate the brain activation during the motor performance. T-statistic values were obtained for each subject and each channel (1st level analysis). A threshold of T-values was set at a p-value of 0.05 for each subject. In so doing, GLM provides the intrinsic statistical significance of the above-threshold T-values obtained.

C. Functional Tasks

Healthy subjects were laid in a stretcher, and they were asked to perform non-paced repetitive finger movements with their right hand, contralateral to the measurement on the left hemisphere. The activation task was organized in 28 blocks, each of them lasting 31 s. Activation blocks were interleaved by rest intervals lasting 29 s. Together with an initial baseline and a final recovery period, the total protocol duration was approximately 30 min. In the Simple Task (ST), the subjects were asked to repeat two subsequent adductions of the index and middle finger. The Complex Task (CT) consisted of repetitions of a specific sequence of movements with their right hand fingers, i.e. two subsequent adductions of the thumb, ring, index, little and middle fingers.

Patients were asked to perform handgrip movements with both their right and left hands in two different trials. The optode pad was mounted over the respective contralateral hemisphere. The first of the two trials was randomized with respect to hemisphere. Each trial was organized in 15 or 20 blocks, respectively, each of them lasting 31 s. Activation blocks were interleaved by rest intervals lasting 29 s. One trial for the right and one for the left sides were performed. The interval between the two trials was approximately 30 min.

D. Subjects

A total of 22 healthy subjects participated in the study. The datasets of those 12 of them who fully accomplished at least 28 trials (i.e. task repetitions) in both the ST and CT were included in the present analysis.

Fourteen patients with recent diagnosis of ischemic stroke participated in the experiment. Eight fully accomplished the handgrip task with both the right and left hands in at least two different sessions. 7 patients had the right brain hemisphere damaged (one left). The best measurement among the two repetitions was chosen for further analysis.

III. Results

For all subjects and patients of the study, HbO and HbR time series were obtained for the *integral* and *variance*. Then, GLM was applied, separately for the two data sets. In the ST, eleven out of twelve subjects provided significant T-values for activation (for both HbO and HbR) for at least one channel of the *variance* set. Nine of them showed no significant T-values for activation based on *integral* at all, two for HbR only. In only one case significant activation was observed for the *integral* track, and no activation for *variance*. In the CT, eleven out of twelve subjects provided significant T-values for activation (for both HbO and HbR) for at least one channel of the *variance*. For eight of them, no significant T-values were found in the *integral* at all, for the other three subjects *integral* revealed significant T-values for HbR only. One subject could not provide any significance at all, thus implying that GLM failed in detecting activation. In this last case, visual inspection of the tracks revealed very poor synchronization of HbO and HbR variations with the task design.

To compare the results for both tasks, the channel with best activation was separately chosen for the ST and CT for each subject, on the basis of block-averaged NIRS tracks. Once chosen, GLM T-statistic values for HbO and HbR were plotted in two different graphs (see Fig. 2), by means of bar representations. In the comparison between HbO in ST and CT, nine healthy subjects out of twelve showed higher T-values of the GLM statistics for the CT. In two cases, values were comparable, and in one case only the ST was paired with a higher T-value (Fig. 2 left). HbR showed a similar trend, with GLM performing more robustly for the CT in eight cases out of twelve (Fig. 2 right). In only one case, though, results showed a clearly opposite trend.

Another goal of our analysis was to check whether a significant activation revealed by the GLM analysis was correlated with a high amplitude of the trNIRS *variance* signal. The joint investigation of GLM T-values and of the amplitudes of the HbO change related to the task showed strong positive correlation (Fig. 3 left). In the CT, moreover, very high values of HbO amplitude change still matched with the highest values of T-statistics. This fact was further confirmed by the plot of T-statistics vs. amplitude of HbR changes related to the task (Fig.3 right). Indeed, in the case of HbR decrease, correlation between T-values and the modulus of HbR changes is still observed. One subject only showed a positive change of HbR related to the task, which clearly stands apart.

Patients were investigated by comparing GLM statistics over the injured and non-injured sides. Fig. 4 depicts the results for HbO and HbR during a handgrip task. In six cases out of eight, GLM could detect HbO activation, by providing above-threshold or close-to-threshold T-values for functional activation, in at least one channel. In one case (pat. 7), GLM provided good statistical results for the non-injured side, but a very low T-value for the injured side, indicating a possible lack of functional activation over the injured side. In one single case (pat. 2), GLM performed poorly over both hemispheres. GLM could provide above-threshold statistics for HbR over both injured and non-injured sides for only four patients out of eight. Patient 7 showed statistic values similar to those obtained for HbO, putting forward an organic origin for the lack in HbR detection over the injured hemisphere. In other three cases, GLM found above-threshold values for HbR over the non-injured hemisphere, and below-threshold values over the injured hemisphere.

The joint study of GLM T-statistics and HbO amplitude changes related to the task showed that the strong positive relation found between the increase in HbO variation (i.e. the increase of activation) and the value of T-statistics was verified for patients as well (Fig. 5 left). This fact was also observed in the plot of T-statistics and of the HbR amplitude changes related to the task (Fig. 5 right). Indeed, in the case of HbR decrease, a correlation between T-statistics and the modulus of HbR changes is still observed. One subject only showed high value of the T-statistics in combination with the absence of HbR amplitude. This is probably due to artifacts in the NIRS recordings.

IV. Discussion

GLM processing provided strong evidence that the consideration of the variance signal derived from trNIRS measurements is beneficial in the disentanglement of cortical activation from the overall (cw) received signal. This fact also confirms that trNIRS leads to more accurate results compared to cwNIRS, and can separate cortical functional activation (largely selected by *variance* tracks) from systemic superficial hemodynamics (which are often dominating the *integral* signal).

Overall, the healthy subjects showed higher T-values of GLM statistics for the CT with respect to the ST. This result could be due to two different causes.

(i) CT induced larger changes in the HbO and HbR time series with respect to ST, which was mirrored by higher amplitudes of changes derived from the block-averaged time tracks,

(ii) It is also possible that the regressor, modeling the experimental time course as an on/off function convolved with HRF, better fitted the data of the CT.

In any case, task complexity, thus, introduces some enhancement for the functional activation.

Comparing T-values and amplitudes from block-averaged signals, a strong correlation for HbO as well as HbR was observed, and for both healthy group and stroke patients. This correlation shows that the results of both analyses are consistent, apart from single cases which need further clarification. However, compared to the simple block average, the more advanced GLM analysis assesses the full time series, and it is capable of providing significance values.

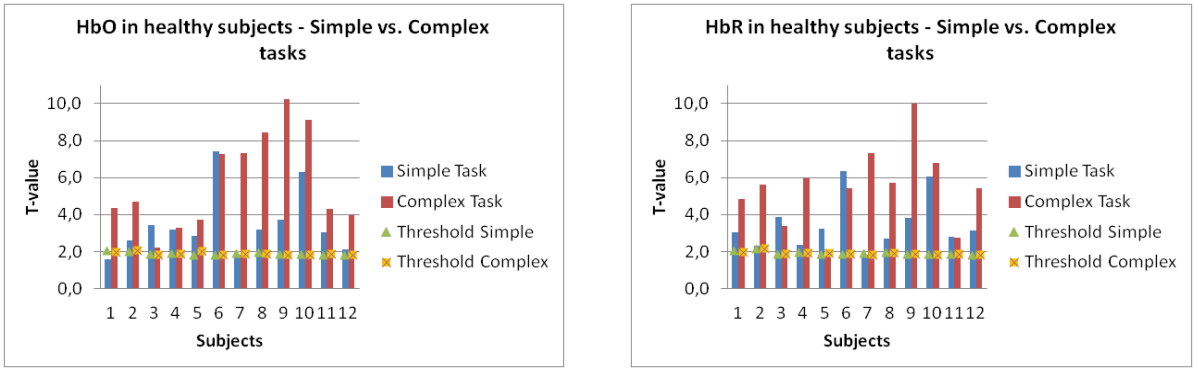


Figure 2. Values of GLM T-statistics, calculated for HbO (left) and for the HbR (right) variance signals, and for the Simple and Complex Tasks for 12 healthy subjects. T-values are shown by blue bars for the Simple Task and red bars for the Complex Task. Thresholds of T-value, set at significance of 0.05, are marked with a green triangle for the Simple Task, and with a yellow square for the Complex Task..

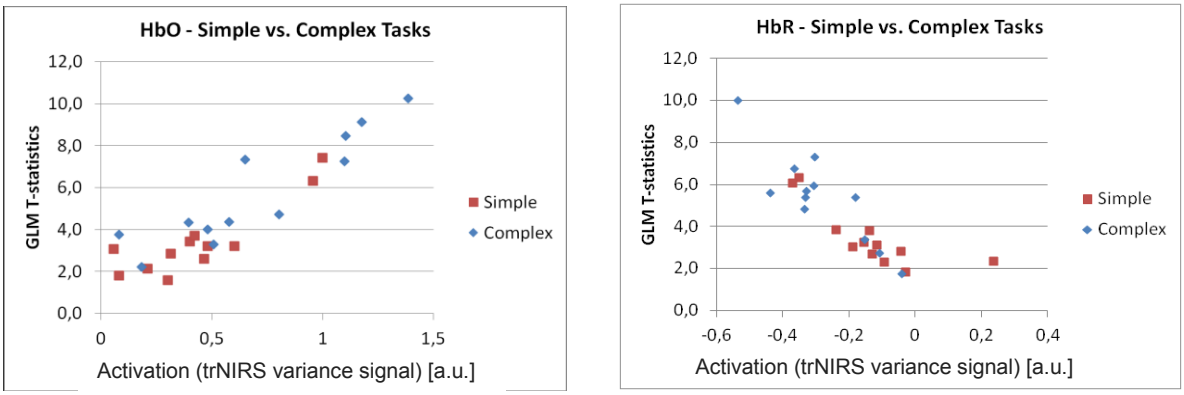
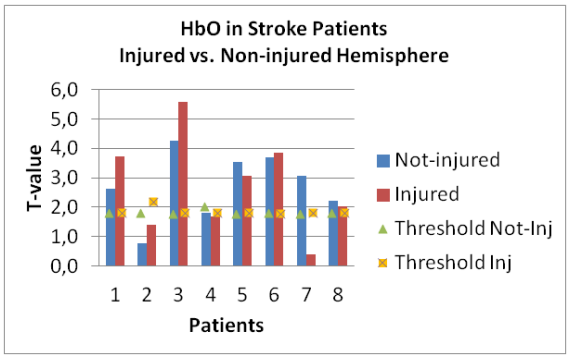


Figure 3. Amplitudes of activation, obtained from the block-averaged HbO (left) and HbR (right) time tracks derived from the variance signal, are plotted against values of GLM T-statistics, calculated for the Simple and Complex Tasks, for the twelve healthy subjects analyzed. GLM performance shows a positive trend with the increase of amplitude for HbO, and a positive trend with the increase of the amplitude modulus for HbR.



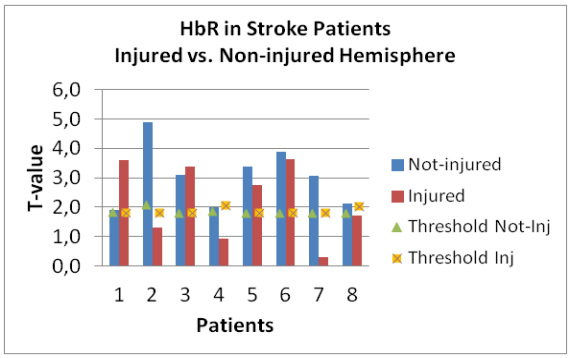
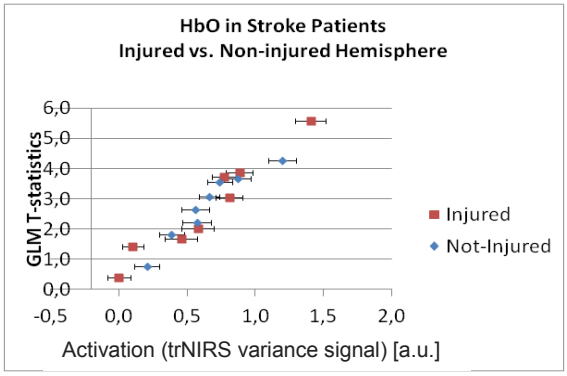


Figure 4. Values of GLM T-statistics, calculated for HbO (left) and HbR (right) variance signals, and for the injured and healthy sides in eight patients with stroke. T-values are shown by blue bars for the healthy hemisphere and red bars for the injured hemisphere. Thresholds of T-value, set at significance of 0.05, are marked with a green triangle for the healthy side and with a yellow square for the injured side.



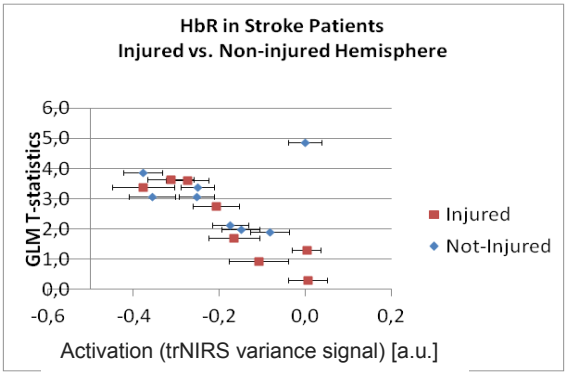


Figure 5. Activation amplitudes, obtained from the block-averaged HbO (left) and HbR (right) time tracks derived from the variance signal, are plotted against values of GLM T-statistics, calculated for the injured and non-injured hemispheres in the eight stroke patients. GLM performance shows a positive trend with the increase of amplitude for HbO, and a positive trend with the increase of the modulus of amplitude for HbR.

Last, GLM was successfully applied for the detection of functional activation in stroke brain. In the case of HbO detection, GLM performance was good in five out of eight patients, regardless of the injury presence. In only one case GLM performed poorly, regardless to the injured or non-injured side, and in just one case the performance was strikingly worse over the injured side. On the other hand, HbR detection showed less stability, with respect to the lesion site: indeed, in three cases T-values were clearly lower for the non-injured hemisphere. This fact points out that (i) GLM seems to be less robust for the detection of HbR over the injured hemisphere, and (ii) HbR functional response could have variability in shape, or could be more prone to change due to the close presence of the lesion. These findings will drive our further work on the application of GLM to functional studies of stroke using the NIRS technique.

V. Conclusion

Our results of the comparative GLM analysis for motor tasks in healthy subjects emphasize the clear advantage or trNIRS, in particular the *variance* signal, compared to the cw technique in retrieving brain activation. We also obtained preliminary evidence of the capability of the trNIRS technique to detect functional activation in stroke brains. Results such as those presented here open an intriguing scenario for the detection of residual functional activation after brain damage with portable techniques. However, reliability of results and certainty in interpretation have to be further studied before trNIRS can become a valuable tool for routine use in clinics.

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